"A PROSPECTIVE, OBSERVATIONAL STUDY ON PREVALENCE OF CARDIOVASCULAR RISK FACTORS AND STATIN USE IN PATIENTS WITH EPILEPSY AND ASSESSMENT OF QUALITY OF LIFE"

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ABBREVIATIONS

AAN	**:** American Academy of Neurology
ADRs	**:** Adverse Drug Reactions
AEDs	**:** Anti-Epileptic Drugs
ANOVA	**:** Analysis of Variance
CBZ	**:** Carbamazepine
CLB	**:** Clobazam
CLN	**:** Clonazepam
CNS	**:** Central Nervous System
CPS	**:** Complex Partial Seizures
CVRF	**:**Cardiovascular risk factor
DDD	**:** Defined Daily Dose
EEG	**:** Electroencephalogram
FDA	**:** Food and Drug Administration
FRS	**:** Framingham risk score
GABA	**:** Gamma(ϒ)-Amino Butyric Acid.
GBP	**:** Gabapentin
GAT-1	**:** GABA Transporter Protein-1
GTCS	**:** Generalized Tonic Clonic Seizures
IERB	**:** Institutional Ethical Review Board

ILAE	**:** International League Against Epilepsy
NICE	**:** National Institute of Clinical Excellence
LEV	**:** Levetiracetam
LTG	**:** Lamotrigine
OPD	**:** Outpatient Department
OXC	**:** Oxcarbazepine
QOL	**:** Quality of Life
PB	**:** Phenobarbitone
PDD	**:** Prescribed Daily Dose
PHT	**:** Phenytoin
PWE	**:** Patient with epilepsy
QOLIE-31	**:** Quality of Life in Epilepsy Inventory 31
QOLIE-10	**:** Quality of Life in Epilepsy- 10
SD	**:** Standard deviation
SES	**:** Socioeconomic Status
TDM	**:** Therapeutic Drug Monitoring
TPM	**:** Topiramate
VPA	**:** Valproic Acid
ZON	**:** Zonisamide

INTRODUCTION

Epilepsy is a disorder that is best viewed as a symptom of disturbed electrical activity in the brain caused by a wide variety of etiologies. It is a collection of many different types of seizures that vary widely in severity, appearance, cause , consequences, and management.

(1) Epilepsy is a common medical and social disorder or group of disorders with unique characteristics .The word "epilepsy" is derived from latin and Greek words for " seizures " or " to seize upon".

Epilepsy has been reported to affect between 5 to 10 people per 1000 and the incidence in developed countries is around 50/100,000/year. It is estimated that 30% of those with epilepsy have recurrent seizures despite optimal antiepileptic therapy.

An epileptic seizure is a transient paroxysm of uncontrolled discharges of neurones causing an event that is discernible by the person experiencing the seizure or by an observer. The tendency to have recurrent attacks is known as epilepsy; by definition, a single attack does not usually constitute epilepsy. Epileptic seizures or attacks are a symptom of many different diseases, and the term epilepsy is loosely applied to a number of conditions that have in common a tendency to have recurrent epileptic attacks.

A patient with epilepsy will show recurrent epileptic seizures that occur unexpectedly and stop spontaneously. Epilepsy is also remarkably uniformly distributed around the world. There are no racial, geographical or social class boundaries. It occurs in both sexes, at all ages, especially in childhood, adolescence and increasingly in ageing populations. The periodic clinical features of seizures are often dramatic and alarming, and frequently elicit fear and misunderstanding. This in turn has led to profound social consequences for sufferers, which has greatly added to the burden of this disease(2).

In ancient times, epileptic attacks were thought to be the result of invasion and possession of the body by supernatural forces, usually malign or evil influences, requiring exorcism, incantations or other religious or social approaches. Today, seizures are viewed as electromagnetic discharges in the brain in predisposed individuals, attributable in part to putative genetic factors, underlying neurological disorders, and largely unknown neurochemical mechanisms.

A wide range of different seizure types and epilepsy syndromes have been identified. Patients are now treated with pharmacotherapy, occasionally with neurosurgical techniques, as well as with psychological and social support. Epilepsy has many causes, but in most patients a cause cannot be identified. Among the pathologies most commonly considered to give rise to epilepsy are cerebrovascular lesions, perinatal or postnatal trauma, infections of the CNS, and tumours or congenital malformations of the brain. This area is referred to as the epileptogenic lesion. The epileptogenic zone is where the seizures actually begin, and this area is usually in or near the epileptogenic lesion. The function of nerve cells and their circuits in the epileptogenic zone has been fundamentally altered, and some even destroyed, by the pathology.

During an epileptic seizure, neurons in the epileptogenic zone begin to discharge hypersynchronous electrical signals at an excessively high rate or in an abnormal pattern. An epileptic seizure can originate only in structures of the brain (e.g. the cerebral cortex and amygdala) but the seizure may then spread to other structures of the CNS (e.g. the basal ganglia). Once a patient has developed epilepsy, individual seizures may be precipitated by a number of conditions and circumstances.

EPIDEMIOLOGY

WHO and International League against Epilepsy (ILAE) have estimated that 34 million out of 50 million people with epilepsy live in developing countries and nearly 80% of them are not on treatment. It is estimated that in India with a population of over 1.5 billion there will be around 6-10 million people with epilepsy, accounting for nearly 1/5th of global burden. The paucity of medical infrastructure, economic concerns and socio-cultural attitudes are known to be a hindrance to the optimal care of epilepsy in these countries.[(4)]

Neuroepidemiology is the study of the distribution and determinants of neurological diseases in human population . While the clinician is concerned with disease in the individual patient, the epidemiologist is concerned with the occurrence of disease within a community. Epidemiological information benefits health policy-makers, public health officials, medical practitioners and patients, the pharmaceutical industry and other epidemiologists.

AETIOLOGY

Epileptic seizures are produced by abnormal discharges of neurones that may be caused by any pathological process which affects the cortical layer of the brain. The idiopathic are those in which there is a clear genetic component, and they probably account for a third of all new cases of epilepsy. In a significant proportion of cases, however, no cause can be determined and these are known as the cryptogenic epilepsies. Possible explanations for cryptogenic epilepsy include as yet unexplained metabolic or biochemical abnormalities and microscopic lesions in the brain resulting from brain malformation or trauma during birth or other injury. The term 'symptomatic epilepsy' indicates that a probable cause has been identified. The likely aetiology of epilepsy depends upon the age of the patient and the type of seizure. The commonest causes in young infants are hypoxia or birth asphyxia, intracranial trauma during birth, metabolic disturbances and congenital malformations of the brain or infection.

In young children and adolescents, idiopathic seizures account for the majority of the epilepsies, although trauma and infection also play a role. In this age group, particularly in children aged between 6 months and 5 years, seizures may occur in association with febrile illness. These are usually short, generalised tonic clonic convulsions that occur during the early phase of a febrile disease. They must be distinguished from seizures that are triggered by central nervous system infections which produce fever, for example, meningitis or encephalitis. Unless febrile seizures are prolonged, focal, recurrent or there is a background of neurological handicap, the prognosis is excellent and it is unlikely that the child will develop epilepsy. The range of causes of adult-onset epilepsy is very wide. Both idiopathic epilepsy and epilepsy due to birth trauma may also begin in early adulthood. Other important causes are head injury, alcohol abuse, cortical dysplasias, brain tumours and cerebrovascular diseases. Brain tumours are responsible for the development of epilepsy in up to a third of patients between the ages of 30 and 50 years. Over the age of 50 years, cerebrovascular disease is the commonest cause of epilepsy, and may be present in up to half of patients.

CLASSIFICATION OF EPILEPSY[1]

People with epilepsy have recurring seizures that often occur spontaneously and without warning. The official definition of a seizure is "a transient occurrence of signs and symptoms due to an abnormal, excessive or synchronous neuronal activity in the brain."

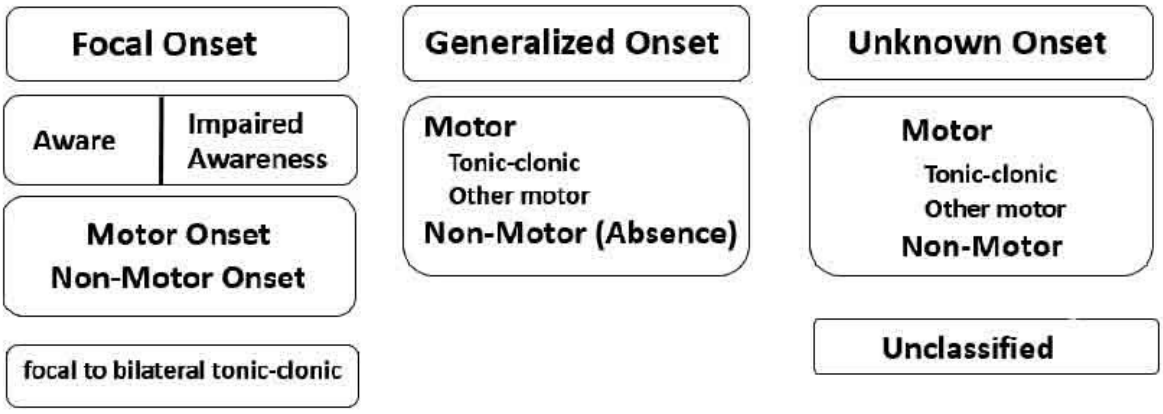
This means that during a seizure, large numbers of brain cells are activated abnormally at the same time. It is like an "electrical storm" in the brain.

The nature of the seizures depend upon many factors, such as the person's age, the sleep-wake cycle, prior injuries to the brain, genetic tendencies, medications, which circuits in the brain are involved, and many others.

Separating seizures into different types helps guide further testing, treatment, and prognosis or outlook. Using a common language for seizure classification also makes it easier to communicate among clinicians caring for people with epilepsy and doing research on epilepsy. The classification also provides common words for people with epilepsy and the general public to describe seizures. The basic classification is a simple version of the major categories of seizures. The first step is to separate seizures by how they begin in the brain.

The classification begins by dividing seizures into those that start focally, meaning involving circuits (networks) in one hemisphere or side of the brain versus those that engage networks in both sides of the brain at the onset.

If onset is unknown, the seizure falls into the unknown onset category. Later on, the seizure type can be changed if the onset of a person's seizures becomes clear. The type of seizure onset is important because it affects choice of seizure medication, possibilities for epilepsy surgery, outlook, and possible causes.



Describing motor and other symptons in focal seizures: Many other symptoms may occur during a seizure. In this basic system, seizure behaviors are separated into groups that involve movement.

A focal motor seizure means some type of movement occurs during the event. For example, twitching, jerking, or stiffening movements of a body part or automatisms (automatic movements such as licking lips, rubbing hands, walking, or running).

A focal non-motor seizure includes other symptoms such as changes in sensation, emotions, thinking, or experiences. A seizure therefore can be focal motor (the word "onset" is implied) or focal non-motor, for example, focal sensory, with or without mention of awareness. It is also possible for a focal aware or impaired awareness seizure to be sub-classified as motor or non-motor onset.

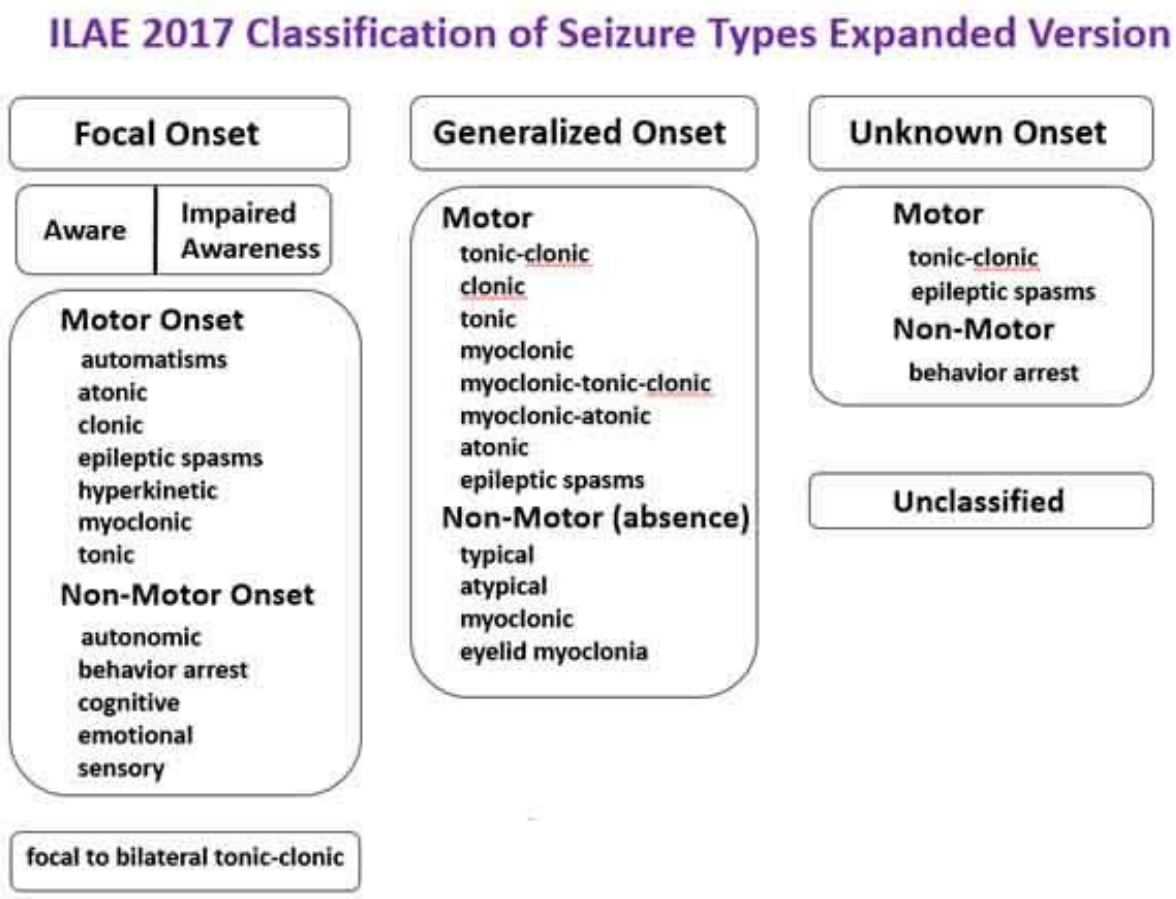
Describing generalized onset seizures: Seizures that start in both sides of the brain, called generalized onset, can be motor or non-motor (absence).The generalized tonic-clonic seizure term is still used to describe seizures with stiffening (tonic) and jerking (clonic). This loosely corresponds to "grand mal."

The generalized absence seizure corresponds to the old term "petit mal." These seizures involve brief changes in awareness, staring, and some may have automatic or repeated movements like lipsmacking.

THE NEW EXPANDED CLASSIFICATION

The expanded classification keeps the framework of the basic classification, but adds more seizure types as subheadings.

- Focal motor onset seizure types include automatisms, atonic, clonic, epileptic spasm, hyperkinetic, myoclonic and tonic seizures. Several of these types also appear in the generalized onset categories.
- Focal non-motor onset seizures include autonomic, behaviour arrest, cognitive, emotional, and sensory seizures. Since seizures often have several different symptoms and behavioural signs, the seizure is named for the first prominent symptom or sign. This has been the usual clinical practice, because seizure onset marks the part or network of the brain involved in generating the seizure. Other regions become involved as the seizure spreads.



Focal onset seizures may occur with or without impairment of awareness, except that atonic and epileptic spasm seizures usually do not show obvious impairment of awareness.

- Focal automatisms seizure: A seizure with automatic fumbling behaviour, such as lip-smacking, hand-rubbing, picking at objects, walking in circles, repeating meaningless phrases, or undressing.
- Focal atonic seizure: Focal, for example in one arm or leg, sudden loss of muscle tone and strength, resulting in a transiently limp limb.
- Focal clonic seizure: Sustained rhythmically jerking of one part of the body or face.
- Focal epileptic spasms: Sudden flexion or bending of the trunk with flexion or extension of the limbs lasting less than a few seconds. These often occur in clusters. The term infantile spasm applies to epileptic spasms occurring during infancy. Video-EEG monitoring and a brain MRI may be needed to determine whether onset of epileptic spasms is focal or generalized.
- Hyperkinetic seizure: A seizure with vigorous thrashing or pedaling movements. Even though both sides of the body are usually involved with these seizures, the EEG often shows a focal and frontal lobe origin. Some people used to call these hypermotor seizures.
- Focal myoclonic seizure: Irregular and brief lightning jerks of limbs or face on one side of the body.
- Focal tonic seizure: Stiffening of arm, leg, or neck producing a forced posture during the seizure.
- Focal autonomic seizure: A seizure whose primary effect is on autonomic nervous system functions, such as heart rate, blood pressure, sweating, skin colour, hair standing on end (piloerection), and gastrointestinal sensations.
- Focal behaviour arrest seizure: In this seizure type, movement stops, sometimes called a freeze or a pause. Because brief behaviour arrest is common and hard to recognize as being abnormal, a seizure should only be classified as a focal behaviour arrest seizure if the behaviour arrest is the main feature through the entire seizure.
- Focal cognitive seizure: This type of seizure refers to impaired cognition (thinking) during a seizure. The impairment might affect language, spatial perception, ability to calculate math, or other cognitive functions. Do not count loss of awareness or

memory (unless only memory is impaired) as a focal cognitive seizure, because awareness is used to describe other seizure types.

- Focal emotional seizure: This seizure type begins with spontaneous fear, anxiety, or less often joy. There may be involuntary laughing or crying, each of which might or might not be accompanied by a subjective emotion. Gelastic and dacrystic seizures would fit into this group.
- Focal sensory seizure: Sensory seizures can consist of tingling or numbness, visual symptoms, sounds, smells, tastes, tilting or spinning sensations (vertigo), and hot-cold feelings.

Generalized onset seizures are not characterized by level of awareness, because awareness is almost always impaired.

- Generalized tonic-clonic: Immediate loss of awareness, with stiffening of all limbs (tonic phase), followed by sustained rhythmic jerking of limbs and face (clonic phase). Duration is typically 1 to 3 minutes. The seizure may produce a cry at the start, falling, tongue biting, and incontinence.
- Generalized clonic: Rhythmical sustained jerking of limbs and/or head with no tonic stiffening phase. These seizures most often occur in young children.
- Generalized tonic: Stiffening of all limbs, without clonic jerking.
- Generalized myoclonic: Irregular, unsustained jerking of limbs, face, eyes, or eyelids. The jerking of generalized myoclonus may not always be left-right synchronous, but it occurs on both sides.
- Generalized myoclonic-tonic-clonic: This seizure is like a tonic-clonic seizure, but it is preceded by a few myoclonic jerks on both sides of the body. Such seizures are commonly seen in people with the syndrome of juvenile myoclonic epilepsy.
- Generalized myoclonic-atonic: This seizure presents with a few myoclonic jerks, followed by a limp drop. These seizures may be seen in children with Doose syndrome.
- Generalized atonic: This is an epileptic drop attack, with sudden loss of muscle tone and strength and a fall to the ground or a slump in a chair. Atonic seizures usually last only seconds.

- Generalized epileptic spasms: Brief seizures with flexion at the trunk and flexion or extension of the limbs. Video-EEG recording may be required to determine focal versus generalized onset.
- Generalized typical absence: Sudden onset when activity stops with a brief pause and staring, sometimes with eye fluttering and head nodding or other automatic behaviors. If it lasts for more than several seconds, awareness and memory are impaired. Recovery is immediate. The EEG during these seizures always shows generalized spike-waves.
- Generalized atypical absence: Like typical absence seizures, but may have slower onset and recovery and more pronounced changes in tone. Atypical absence seizures can be difficult to distinguish from focal impaired awareness seizures, but absence seizures usually recover more quickly and the EEG patterns are different.
- Generalized myoclonic absence: A seizure with a few jerks and then an absence seizure.
- Generalized eyelid myoclonia: Eyelid myoclonia represents jerks of the eyelids and upward deviation of the eyes, often precipitated by closing the eyes or by light. These may be associated with absence seizures in people with Jeavon's syndrome.

Unknown Onset Seizures

Clinicians using the classification will identify a seizure as focal or generalized onset if there is about an 80% confidence level about the type of onset. This means that there is significant confidence on the seizure onset and type.

Seizures without enough confidence about onset are labeled of unknown onset. The most important seizures of unknown onset are tonic-clonic, epileptic spasm, and behavior arrest (which could be either a focal impaired awareness or absence seizure).If a seizure onset becomes clarified at a later date, the type will change.

DIAGNOSIS[5]

Diagnosing epilepsy can be difficult as it is first necessary to demonstrate a tendency to recurrent epileptic seizures. The one feature that distinguishes epilepsy from all other conditions is its unpredictability and transient nature. The diagnosis of epilepsy is clinical and depends on a reliable account of what happened during the attacks, if possible both from the

patient and from an eyewitness. Investigations may help and the EEG is usually one of them. These investigations, however, cannot conclusively confirm or refute the diagnosis of epilepsy. There are other conditions that may cause impairment or loss of consciousness and which can be misdiagnosed as epilepsy; these include syncope, breath-holding attacks, transient ischaemic attacks, psychogenic attacks, etc. In addition, people may present with acute symptomatic seizures or provoked seizures as a result of other problems such as drug intake, metabolic dysfunction, infection, head trauma or flashing lights (photosensitive seizures). These conditions have to be clearly ruled out before a diagnosis of epilepsy is made. Epilepsy must only be diagnosed when seizures occur spontaneously and are recurrent. The diagnosis must be accurate since the label 'suffering with epilepsy' carries a social stigma that has tremendous implications for the person.

The EEG is often the only examination required, particularly in generalised epilepsies, and it aims to record abnormalneuronal discharges. EEGs have, however, limitations that should be clearly understood. Up to 5% of people without epilepsy may have non-specific abnormalities in their EEG recording, while up to 40% of people with epilepsy may have a normal EEG recording between seizures. Therefore, the diagnosis of epilepsy should be strongly supported by a bona fide history of epileptic attacks. Nevertheless, the EEG is invaluable in classifying seizures. The chance of recording the discharges of an actual seizure during a routine EEG, which usually takes 20–30 min, is slight and because of this, ambulatory EEG monitoring and EEG video-telemetry are sometimes required. Ambulatory EEG allows recording in day-to-day circumstances using a small cassette recorder. EEG video-telemetry is useful in the assessment of difficult cases, particularly if surgery is considered. The person is usually admitted to hospital and remains under continuous monitoring. This is only helpful in a very few cases, and it is best suited for people who have frequent seizures.

Neuroimaging with magnetic resonance imaging (MRI) is the most valuable investigation when structural abnormalities such as stroke, tumour, congenital abnormalities or hydrochephalus are suspected. MRI should be carried out in anyone presenting with partial seizures or where a structural lesion on the brain may be responsible for seizures.

MANAGEMENT

The main treatment goals of epilepsy are to achieve adequate seizure control and minimize side effects to anti-epileptic medications with much less attention being given in the past to the patient's perception of the impact of the disease in everyday life. People with epilepsy face many challenges particularly in the psychosocial realm (anxiety, social stigma, low self esteem, difficulty in driving, unemployment), all of which can impact quality of life (QOL)

The best quality of life is associated with a seizure free state. However, a balance between efficacy and side effects must be reached. With older antiepileptic drugs (AEDs), less than 50% of patients achieve good seizure control. Moreover epilepsy being a chronic condition, the patient can develop significant side effects like sedation, impaired memory etc. Hence some seizure control may have to be sacrificed to improve functioning. The newer AEDs offer alternatives for balancing seizure frequency and drug side effects[(1)].

Providing optimal quality of life goes beyond balancing seizure control and side effects. It involves assessing all concerns of a person regarding issues such as driving, their future, social stigma etc. It is also important to treat the other associated comorbidities like depression, anxiety, neuropsychiatric conditions which can impact the overall Quality of life.

General Approach to Treatment

The following is the updated clinical guidance set by NICE Group (National Institute of Clinical Excellence), U.K regarding initiation of pharmacological therapy .[(6)]

AED therapy should only be started once the diagnosis of epilepsy is confirmed. Treatment with AED is generally recommended after a second seizure except in conditions where the individual has a neurological deficit, the EEG shows unequivocal activity and a structural abnormality is seen in the brain. The decision to initiate AED therapy should be taken between the individual, their family (as appropriate) and the specialist after a full discussion of the risks and benefits of treatment which should take into account details of the individual's epilepsy syndrome, prognosis and lifestyle.

It is recommended that individuals should be treated with a single antiepileptic drug (Monotherapy) wherever possible. If the initial treatment is unsuccessful, then monotherapy using a second drug can be tried. If an AED has failed due to adverse effects or continued

seizures, then a second drug is started (which is an alternative first line or second line drug) and built up to an adequate or maximum tolerated dose; then the first drug is slowly tapered.

It is recommended that combination therapy (adjunctive or add on therapy) should only be considered when attempts at monotherapy with AEDs have failed. Combination of drugs with different mechanisms of action is considered advantageous.

Antiepileptic drugs used commonly.

Seizure type	First-line treatment	Second-line treatment
Partial seizures		
	Carbamazepine	Topiramate
	Lamotrigine	Valproate
	Oxcarbazepine	Clobazam
	Levetiracetam	Zonisamide
		Pregabalin
		Phenytoin
		Gabapentin
		Lacosamide
		Eslicarbazepine
Generalised seizures		
Tonic clonic	Valproate sodium	Lamotrigine
Tonic	Carbamazepine	Clobazam
Clonic	Lamotrigine	Phenobarbital
Absence	Ethosuximide	Clonazepam
	Sodium valproate	Lamotrigine
Atypical absences	Sodium valproate	
Atonic	Clonazepam	Lamotrigine
	Clobazam	Carbamazepine
		Phenytoin
		Acetazolamide
		Topiramate
Myoclonic	Sodium valproate	Levetiracetam
	Clonazepam	Acetazolamide
		Topiramate

ASSESSMENT OF CARDIOVASCULAR RISK AND STATIN USE

Some studies have tried to identify an association between CVRFs and epilepsy, however the results and observations have been inconsistent.

Statins are the most popular cholesterol-lowering agents and can be beneficial in the treatment of hypercholesterolemia and other related diseases. Statins act by reducing the hepatic cholesterol biosynthesis and upregulation of LDL-C receptors on the surface of hepatocytes, which then leads to enhanced removal of LDL-C from circulation. Statins also exert pleiotropic actions such as reducing the accumulation of esterified cholesterol into macrophages, increasing endothelial nitric oxide synthetase, decreasing inflammation, and increasing the stability of the atherosclerotic plaque

IMPORTANCE OF QUALITY OF LIFE STUDIES

The growing recognition of the importance of assessing the effects of epilepsy on psychosocial functioning has led to the need to define and quantify quality of life in affected individuals. Quality of life (QOL) is a subjective issue and one that is determined from the patient's point of view depending on clinical, psychosocial and demographic variables.[7]

Measuring the outcome of treatment of epilepsy traditionally has been in the realm of the health care provider, who assesses results of treatment by using seizure frequency and severity, adverse effects, and antiepileptic drug (AED)-level parameters**.** Patient perceptions of outcome often include additional parameters that encompass the effects of epilepsy on daily activities and functions[8] **.** This expanded scope of impact was defined by the World Health Organization (WHO) as health-related quality of life: "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity".

Surveys of patients and physicians have confirmed the usefulness of these screening questions in improving communication and raising issues between patients and providers **.** To improve the specificity of information, generic questionnaires need to be tailored for special populations (e.g., persons with epilepsy) with supplementary items pertinent to problems typically reported by that population[9].

QOLIE-10 QUESTIONNAIRE[12]

It is a brief questionnaire to screen aspects of health-related quality of life for persons with epilepsy. The QOLIE- 10 is a simple screening questionnaire that can be completed easily and quickly by patients. The 10 items fall into three distinct topics as (a) medication effects, (b) mental health, and (c) role functioning and seizure worry, all of which pertain to aspects of daily living for persons with epilepsy.

The QOLIE-I0 provides individual patients with an opportunity to denote epilepsy-related problems and express their concerns to health-care providers. Unlike diagnostic or laboratory individual functions in the real world (e.g., work and social opportunities, transportation, independent living, worry about seizures).

Screening data have several clinical applications for quality of life: (a) alert physician and clinic staff to common patient concerns, (b) inform patients of problems common for this disorder, and (c) facilitate interaction between and decision making by patient and physician.[13]

The QOLIE-10 screening questionnaire includes 11 questions. Three questions have opposite response sets, requiring reverse-scoring. The scoring should be calculated so that all positive responses are lower numbers and all negative responses are higher numbers. The responses obtained are subjected to the scoring tool. The Mean Score is the sum of scores for all questions divided by the number of items answered. The Mean Score is multiplied by the response for Item 11 to create the final "weighted" score[14]. If one item is missing, the score may be imputed based on the 9 responses. If more than one item is missing, the instrument is not valid. Higher scores represent better quality of life [15].

STATIN USE IN PWE

Antiepileptic drugs, including carbamazpine, phenytoin, and phenobarbital, are among the most commonly-prescribed medications for seizres throughout the world. Evidence indicates that these agents, probably via their widespread impact upon the cytochrome P450 system, engender a host of metabolic derangements, including elevations of serum lipids and other serologic markers of vascular risk.[16] These effects would be expected to materially increase the risk of vascular disease, based upon estimation from population studies in the cardiovascular literature, and additional surrogate markers.[17]

The enzyme-inducing AEDs phenytoin (PHT), phenobarbital (PB), carbamazepine (CBZ), and primidone (PRM) increase the activity of the hepatic cytochrome P450 system, which is involved in synthesis of serum cholesterol. Animal data show that a particular enzyme, CYP51A1, catalyzes the conversion of lanosterol into cholesterol intermediates .When these intermediate build up through inhibition of the enzyme, they in turn inhibit the rate-limiting step of cholesterol synthesis, 3-hydroxy-3-methylglutaryl-coenzyme A reductase[(18)], and slow the synthesis of cholesterol. It follows that induction of CYP51A1 should therefore increase cholesterol production through metabolism of these intermediates and reduced feedback inhibiton[(19)].

While the pathway has not been explicitly studied in humans to our knowledge, this mechanism engenders some predictions regarding the effects of certain AEDs in patients. For example, an enzyme-inducing AED such as CBZ should increase serum cholesterol. On the other hand, valproic acid (VPA), an enzyme-inhibiting medication, should decrease metabolism of intermediates and increase feedback inhibition, thereby decreasing production of cholesterol.

The discovery of a class of drugs, the statins, which selectively inhibit 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase) was a significant advance in the treatment of dyslipidaemia. Their primary site of action is the inhibition of HMG-CoA reductase in the liver and the subsequent inhibition of the formation of mevalonic acid, the rate-limiting step in the biosynthesis of cholesterol. This results in a reduction in intracellular levels of cholesterol, an increase in expression of hepatic LDL receptor, and enhanced receptor-mediated catabolism and clearance of LDL-C from serum.

The statins are a heterogeneous group metabolised by different CYP450 isoenzymes. Simvastatin, atorvastatin and lovastatin are metabolised by CYP3A4, fluvastatin is metabolised by CYP 2C9, and pravastatin and rosuvastatin are eliminated by other metabolic routes and less subject to interactions with CYP450 isoenzymes than other members of the family. Nevertheless, caution is still required as a 5- to 23-fold increase in pravastatin bioavailability has been reported with ciclosporin. Simvastatin and atorvastatin do not alter the activity of CYP3A4 themselves, but their serum levels are increased by known inhibitors of CYP3A4.

In patients receiving a statin, a once-daily regimen involving an evening dose is often preferred. Several of the statins (fluvastatin, pravastatin, simvastatin) are claimed to be more

effective when given as a single dose in the evening compared to a similar dose administered in the morning. This has been attributed to the fact that cholesterol biosynthesis reaches peak activity at night. However, atorvastatin and rosuvastatin may be taken in the morning or evening with similar efficacy.

ASSESSMENT OF CARDIOVASCULAR DISEASE RISK

The Framingham risk score (FRS) is a simplified and common tool for the assessment of risk level of CAD over 10 years . The FRS considers six coronary risk factors, including age, gender, total cholesterol (TC), high density lipoprotein cholesterol (HDL), smoking habits, and systolic blood pressure. FRS is the most applicable method for predicting the person's chance of developing cardiovascular disease (CVD) in long term[(20)].

FRS was used to investigate the risk of cardiovascular disease. FRS scores were calculated based on the six coronary risk factors including age, gender, TC, HDL-cholesterol, systolic blood pressure, and smoking habits. The cutoffs for calculating FRS were as follows:
TC < 160, 160–199, 200–239, 240–279, and ≥ 280 mg/dL; for systolic blood pressure: < 120, 120–129, 130–139, 140–159, and ≥ 160 mmHg; and for HDL-C: < 40, 40–49, 50–59, and ≥ 60 mg/dL . Ten-year risk in percentage was calculated by total points (1 point 6%, 2 points 8%, 3 points 10%, 4 points 12%, 5 points 16%, 6 points 20%, 7 points 25%, 10 points or more > 30%). Absolute CVD risk percentage over 10 years was classified as low risk (< 10%), intermediate risk (10–20%), and high risk (> 20%)[(21).]

ABSTRACT

The work entitled " A prospective, observational study on prevalence of cardiovascular risk factors and statin use in patients with epilepsy and assessment of quality of life*"* was conducted in the department of neurology of a 1000 bedded multispecialty hospital .The study protocol was prepared and submitted to the ethical committee of the hospital and official approval was obtained to carry out the study after ensuring the scope of the study in the department of neurology of the study hospital. After receiving the official approval, the study was conducted for a period for a period of nine months from December 2017 to August 2018. A total of 130 cases with epilepsy were collected. Prior consents from the patients were taken after explaining them the need of the study.

The analysis of the study conducted for eight months revealed that there were 79(61%) male patients and 51 (39%) female patients who fit into the inclusion criteria. The age categorization of the study population indicated that maximum number of patients are between the age group of 51-65 (36%) followed by age group of 35-50 (32%). Hypertension (28%) and Diabetes(18%) were the major comorbid conditions among epilepsy patients. Patients with smoking (11%) and drinking (7%) habits were also documented during the study. No patients with previous coronary artery disease were included in the study. The majority of the patients were known cases of epilepsy for more than a year (83%). The majority of the patients were diagnosed with generalised tonic clonic seizures (37.5%), followed by partial seizures with secondary generalisation(31%).

To find out any rationality in therapy, an attempt was made to know about the concurrent drugs prescribed. The results revealed that proton pump inhibitors (89%), antibiotics (51%), lipid lowering agents (52%) and antiemetics (58%) were the major category of drugs prescribed. Antidiabetic drugs (16%) and antihypertensive drugs (26%) dr were major category of drugs prescribed since high prevalence of hypertension and diabetes was observed as comorbidity in the study population. Levetiracetam (84%), was the maximum prescribed antiepileptic drug in the study department, followed by fosphenytoin (32%),lacosamide (24%) and clobazam (20%).The drug interaction between atorvastatin and pantoprazole was the mostly recorded drug interaction,which was observed in 15 patients with moderate severity. Among the study population 85(65%) patients were receiving polypharmacy and 45(35%) patients were receiving monotherapy. A total of 68(52%) of

patients were receiving lipid lowering drugs, in which 51(39%) patients were having lipid profile data.

The health related quality of life of epilepsy patients were assessed by direct interviewing the patients with QOLIE-10-P questionnaire. The QOLIE-I0-P questionnaire provided individual patients with an opportunity to denote epilepsy-related problems and express their concerns to health-care providers. The brevity of this screening tool has the potential of saving time without sacrificing the quality of information collected or interfering with the relationship between the patient and the researcher. The QOLIE- 10-P questionnaire is a simple screening questionnaire that can be completed easily and quickly by patients. The 10 items fall into three distinct topics as (a) medication effects, (b) mental health, and (c) role functioning and seizure worry, all of which pertain to aspects of daily living for persons with epilepsy. The 11^{th} question enables the patient to express his feelings on the burden of epilepsy on his/her normal life.

The scoring tool for QOLIE-10-P questionnaire was obtained from the QOLIE development group and used. The mean score of the first 10 questions were calculated and its mean was multiplied with the score obtained for the 11^{th} question to produce the weighted final score.

LITERATURE REVIEW

Martin J. Brodie et al (2018) published The International League against Epilepsy (ILAE) published in the April 2017 edition of *Epilepsia* three companion articles on the classification of seizures and the epilepsies. These represent a long-awaited update on the original 1981 and 1989 publications and provide a modern descriptive template. The new classification presents three levels of terminology, involving seizure types, epilepsy types, and syndromes. In this fourth paper, we present an interpretation of thesenewconcepts for people with epilepsy and those who care for them, as well as for young medical doctors not specialized in epilepsy and nurses. Our goal in writing this paper is to ensure that everyone is speaking and understanding the same language, which is fundamental to the optimal management of people with epilepsy.

Prakruti Patel et al (2017) undertaken a study to measure efficacy and tolerability of antiepileptic drugs in patients of epilepsy with a particular reference to the impact on quality of life (QOL). The efficacy of the drug therapy was calculated by counting the number of seizure per month using seizure diary. QOL was measured using Quality of Life in Epilepsy-31-P questionnaire .Antiepileptic drugs are efficacious in treating and improving the quality of life of patients suffering from epilepsy.

Dong Wook Kim et al (2017) performed a study to assess the effects of lifestyle modification and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor (statin) therapy on the increased circulatory markers for vascular risk in patients with epilepsy. The circulatory markers of vascular risk were measured twice before and after a 3-month intervention. There were no reports of serious adverse events or seizure aggravation related to the statin treatment. Our findings suggest that lifestyle education is necessary in patients with epilepsy with increased vascular risk and that treatment with statin would be a well-tolerated and effective option for these patients.

Leila Jahangiry et al (2017) conducted a study evaluating the predictive value of Framingham risk score (FRS) for cardiovascular disease (CVD) risk assessment in patients with metabolic syndrome in Iran. Because of the emerging high prevalence of CVD among Iranian population, it is important to predict its risk among populations with potential predictive tools. Therefore, the aim of the current study is to evaluate the FRS and its determinants in patients with metabolic syndrome. In the current study, significant

associations between components of metabolic syndrome and different FRS categorization among patients with metabolic syndrome were identified. High SBP and FSG were associated with meaningfully increased risk of CVD compared with other parameters.

Halley B. Alexander et al(2017) conducted a study to evaluate the effects of AED polypharmacy on QOL while accounting for seizure status and other potential covariates. The purpose of the study was to determine the association of polypharmacy with QOL. Two hundred seven patients with epilepsy were surveyed on characteristics within the last 4 weeks: QOL Quality of Life in Epilepsy-Patient-Weighted (QOLIE-10-P) and seizure status (seizure-free or not), demographics, epilepsy characteristics, insomnia, sleepiness, mood, sleep–wake timing, healthcare use, and employment. Those on polypharmacy (antiepileptic drug (AED) N 1) were compared with controls (AED = 1) with univariate comparisons and subsequent multivariate regression. Polypharmacy was associated with worse QOL even after controlling for seizure status. Covariates offered no improvement to the model. Polypharmacy was associated with worse QOL in patients with epilepsy despite seizure control. Further investigation into specific etiology of polypharmacy's influence on QOL is warranted in order to develop paradigms for optimal treatment.

RK Surekha et al (2017) conducted a study to determine the level of health related quality of life of patients with epilepsy in a teaching hospital.The study revealed that patients who were on a single drug(monotherapy) had a much better QOL than the patients on more than one drug(polytherapy).

Green B et al(2017) examined to what extent attachment style and relationship quality with their main informal carer impact on levels of HRQoL, depression, and anxiety in patients with PNES versus those with epilepsy. Patients with PNES reported higher levels of anxiety and depression and lower HRQoL, than those with epilepsy. PNES: No significant correlations were found with HRQoL but depression correlated positively with attachment avoidance, attachment anxiety, and relationship conflict. Anxiety correlated positively with attachment avoidance, attachment anxiety, and relationship conflict, and negatively with relationship depth and support Levels of anxiety and depression were higher in patients with PNES than those with epilepsy. Interpersonal problems were much more closely associated with anxiety and depression in patients with PNES than those with epilepsy. The findings

support the use of therapeutic interventions for PNES focusing on attachment and relationship issues.

Vivanco-Hidalgo et al (2016) conducted a study to compare the prevalence of cardiovascular risk factors (CVRFs), cardiovascular risk and statin use in people with epilepsy (PWE) and the general population. The CVRFs and cardiovascular risk score were compared between 815 PWE from an outpatient register and 5336 participants from a general population cohort. Patients taking enzyme-inducing antiepileptic drugs (EIAEDs) had more dyslipidemia than the general population (41.6% vs. 34.6%) but similar cardiovascular risk. Independently of risk or CVRFs, PWE had 60% more probability of receiving statins than the general population. People with epilepsy had more dyslipidemia, related to EIAEDs, and lower cardiovascular risk but still took more statins than the general population.

Jerzy P. Szaflarski et al (2016) examined the provision of care to older adults with epilepsy and compliance with the "Quality Indicator for Epilepsy Treatment 15" (QUIET-15) measure. Overall, aminority ofMedicare beneficiaries experienced seizure recurrence that resulted in an ER visit. However, only half of themreceived treatment concordantwith QUIET-15. Though racial differences were observed in occurrence of seizures, none were noted in the provision of care.

Altaf Saadi et al (2016) conducted a study to assess the quality of life in epilepsy (QOLIE) among adults in the lower middle-income country of Bhutan and assess the potential demographic and clinical associations with better QOLIE. People with clinically diagnosed epilepsy were prospectively enrolled at the Jigme Dorji Wangchuck National Referral Hospital in Thimphu (2014–2015). Regression models were constructed to assess the potential impact of age, sex, residence in the capital city, wealth quintile, educational attainment, seizure in the prior year, seizures with loss of consciousness, self-reported stigma score, and need for multiple antiepileptic drugs. There are potentially modifiable associations with low QOLIE. Addressing the educational level and self-perceived stigma of PWE may have an especial impact. The low QOLIE in Bhutan may reflect cultural approaches to epilepsy, health services, or other factors including those outside of the health sector.

A Staniszewska et al (2015) conducted a study to identify the demographic and socioeconomic factors that are associated with a poor quality of life in patients with epilepsy. The analysis of variance did not show any significant relation between quality of life and all

subscales QOLIE-31 and sex or driving license. The cognition domain showed the worst scores.

Scott Mintzer et al (2014) undertaken a study to suggest that EIAEDs produce elevation of serum lipids, which could require additional treatment. We assessed the current use of EIAED in monotherapy for epilepsy in the U.S., as well as the correlation between use of EIAEDs and subsequent new prescriptions for HMG-CoA reductase inhibitors ("statins") for hyperlipidemia. EIAED prescription for epilepsy appears to increase with increasing age in the U.S. despite the absence of a cogent rationale for this practice, suggesting a failure to appreciate the complications of EIAED therapy among U.S. physicians. Statins were more often started in those newly-prescribed EIAEDs than to those given non-inducing AEDs. These preliminary data provides further evidence suggesting that EIAEDs elevate lipids in a clinically meaningful manner.

Niki Katsiki et al(2014) studied the association of epilepsy with increased cardiovascular disease (CVD) morbidity and mortality. The exact causes of this link are not clearly defined. The role of antiepileptic drugs (AEDs) in influencing CVD risk in patients with epilepsy remains controversial. A link between epilepsy, AEDs and cardiac arrhythmias has been proposed and may be responsible for sudden unexpected death in epilepsy. We searched MEDLINE up to December 1, 2013 for relevant publications using combinations of keywords. We also examined the reference list of articles identified by this search and selected those we judged relevant. These were included in this narrative review. AEDs may exert both beneficial and adverse cardiovascular effects. This narrative review considers the influence of AEDs on some predictors of vascular. Certain AEDs can also have pro-arrhythmic properties. AEDs may exert different effects on various established and emerging predictors of vascular risk. Furthermore, pharmacokinetic interactions between AEDs and drugs used to reduce vascular risk (e.g. statins) need to be better documented.

NURULUMI AHMAD et al (2013) carried out a study to assess the adherence intention towards pharmacotherapy and its impact on quality of life in epilepsy patients. This study demonstrates that adherence intention has a significant impact on patient quality of life. Therefore, adherence intention should be monitored to provide appropriate support in improving quality of life in epilepsy patients.

Ane Gedde-Dahl et al (2012) performed a study was to compare statin prescription in patients receiving EIAEDs versus non-enzyme-inducing antiepileptic drugs (NEIAEDs), before and after introduction of prescribing restrictions for statins in Norway. The Norwegian Prescription Database was used to extract data on patients using antiepileptic drugs and statins during 2004 and 2008. Statin type and dose used were compared between patients treated with at least one EIAED (i.e., carbamazepine, phenobarbital, phenytoin, primidone) and those receiving NEIAEDs only (i.e., all other antiepileptic drugs). The present study shows that the interaction risk between CYP3A4-metabolized statins and EIAEDs is largely overlooked in Norwegian clinical practice. To avoid therapeutic failure of statin treatment in patients using AEDs, implementation of strategies for systematic management of drug interactions is warranted.

Romy Mahrer-Imhof et al (2012) conducted a study to investigate factors that influence QoL in hospitalized adult patients with epilepsy and their relatives. Epilepsy is not only a neurological disorder but may also have negative psychosocial consequences on people with epilepsy (PWE) and their relatives. Epilepsy has a major impact on quality of life (QoL) in PWE and family members. However, less is known about the impact of family support and family functioning on quality of life for PWE and family members and their interaction. Therefore, the study aimed to investigate factors that influence QoL in hospitalized adult patients with epilepsy and their relatives. The patients' QoL, however, depended significantly on the QoL of the family members. Interventions should address both PWE and family members and focus on the self-care improvement of PWE and the well-being and coping of family members. A patient-centred approach needs to include both the PWE and the relatives and address family support in order to alleviate stress in the patients and relatives alike.

Devender Bhalla et al(2012) carried out a study to Identify epilepsy-associated factors and calculate measures of impact, stigma, quality of life (QOL), knowledge attitude-practice (KAP) and treatment gap in Prey Veng, Cambodia. QOL scores in our population were not better than resource-rich populations which might be due to better healthcare possibilities or with respect to different sociocultural environments

Christoph Helmstaedter et al (2011) conducted a prospective, multicenter, non-interventional surveillance study (ZADE study) which explored seizure outcome and

tolerability of adjunctive treatment with zonisamide (ZNS) in a non-selected sample of patients with partial-onset seizures in everyday clinical practice. Changes in quality of life (QOL) and health status were also recorded. Clinical status was assessed before and 4 months after introduction of ZNS. In conclusion, adjunctive treatment with ZNS seems to be efficacious and well tolerated. QOL improvement was predicted by baseline score, seizure outcome, and overall drug load, and is thus more likely a result of enhanced seizure control, rather than an intrinsic psychotropic effect of zonisamide.

Emilio Perucca et al(2005) carried out a study to understand the clinically relevant drug interactions with antiepileptic drugs. Some patients with difficult-to-treat epilepsy benefit from combination therapy with two or more antiepileptic drugs (AEDs). Additionally, virtually all epilepsy patients will receive, at some time in their lives, other medications for the management of associated conditions. In these situations, clinically important drug interactions may occur. Interactions involving AEDs have not been well characterized, but their understanding is important for a more rational approach to combination therapy. In particular, neurotoxic effects appear to be more likely with coprescription of AEDs sharing the same primary mechanism of action.

Joyce A Cramer et al (1996) conducted am evaluation of a brief questionnaire to screen aspects of health-related quality of life for persons with epilepsy. A study of 304 adults with epilepsy was undertaken at 25 seizure clinics in the United States. It was used for derivation of a brief screening tool from a longer instrument (QOLIE-89). The 10-item questionnaire (QOLIE-10) covers general and epilepsy-specific domains, grouped into three factors: Epilepsy Effects (memory, physical effects, and mental effects of medication), Mental Health (energy, depression, overall quality of life), and Role Functioning (seizure worry, work, driving, social limits). Scale scores were significantly different among seizure groups ($p = 0.003$). The QOLIE-10 can be completed by a patient in several minutes and reviewed rapidly by the physician. This screening tool could provide potentially useful information for initial assessment or follow-up of problem areas that are not commonly evaluated during routine clinical visits with patients with epilepsy.

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SCOPE OF THE STUDY

Epilepsy is one of the oldest conditions known to mankind and still one among the most common neurological conditions affecting individuals of all ages. According to ILAE Guidelines, a person with active epilepsy is one who has had at least one epileptic seizure in the previous five years, regardless of anti-epileptic drug treatment. Epilepsy in remission indicates that the patient has been seizure free for five or more years with or without treatment. All medical conditions that are chronic impact to a greater or lesser degree on the life quality of those affected by them. Epilepsy is a chronic condition characterized by clinical uncertainty. Epilepsy is an example of a medical diagnosis that is retained even when signs and symptoms are well controlled and all laboratory tests are normal.

QOL is a subjective issue and one that is determined from the patient's point of view depending on demographic, clinical and socioeconomic factors. Health-related quality of life (HRQOL) has been defined by WHO as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity". The QOLIE-10-P provides individual patients with an opportunity to denote epilepsy-related problems and express their concerns to healthcare providers. Thus, although it was designed as a screening tool, it can still be scored and used in research.

The overall quality of life is worse in patients with epilepsy than in the general population. It was comparable or worse in patients with epilepsy than that in patients with other chronic conditions; and it was similar to that of healthy persons when patients with epilepsy were well-controlled. QOL is influenced by biological factors as well as cultural, social and religious beliefs and values. QOL of patients with epilepsy depended upon effectiveness of anti-epileptic therapy and disease duration. Due to the special nature and course of the disease, chronic pharmacotherapy and numerous socioeconomic factors influence the quality of patients with epilepsy. The duration of epilepsy may play an important role in QOL, therefore we analysed the relationship between quality of life and duration of disease.

A high frequency seizure rate usually limits the amount of daily activity in patients' everyday lives. This fact leads to impairment of physical activity and social functioning, as well as to psychological problems. Depression and anxiety are common psychiatric symptoms in patients with epilepsy, exerting a profound negative effect on their health-

related quality of life. The adverse effects remain the leading cause of failures in treatment and the major determinant of the impaired health related quality of life in people with epilepsy.

The brevity of this screening tool has the potential of saving physician time without sacrificing the quality of information collected or interfering with the physician-patient relationship. Patients can complete the questionnaire while waiting to be seen, complete it at home and bring it to the next visit, or return it by mail for later use.The QOLIE-I0 provides individual patients with an opportunity to denote epilepsy-related problems and express their concerns to health-care providers. Unlike diagnostic or laboratory tests that report whether a patient's results are within the "normal" range, quality-of-life instruments indicate how an individual functions in the real world (e.g., work and social opportunities, transportation, independent living, worry about seizures).

Asking the patient to complete the QOLIE-10-P before seeing the physician brings fresh information to the clinical interview in a uniform style that could enhance the patient's ability to focus on issues pertinent to epilepsy while economizing on the amount of time the physician needs to cover the range of health-related quality-of-life topics. Antiepileptic drugs are able to alleviate the symptoms but may produce adverse reactions which may also affect the quality of life in epilepsy patients. Therefore, measurement of quality of life is considered vital for the care of epileptic patients. Antiepileptic drugs are efficacious in treating and improving the quality of life of patients suffering from epilepsy. Hence, the choice of therapy depends on the cost of therapy as well as availability and tolerability of the drug in public health care setup. It is recommended that besides providing an optimum drug treatment that relieves the current symptoms of the disease, quality of life should also be considered as a prognostic tool and attempts should also be made to provide a psycho-social support to obtain a significant improvement in quality of life.

Enzyme-inducing antiepileptic drugs (EIAEDs), including carbamazpine, phenytoin, and phenobarbital, are among the most commonly-prescribed medications for seizures throughout the world. Mounting evidence indicates that these agents, probably via their widespread impact upon the cytochrome P450 system, engender a host of metabolic derangements, including elevations of serum lipids and other serologic markers of vascular risk. These effects would be expected to materially increase the risk of vascular disease, based upon estimation from population studies in the cardiovascular literature, and additional

surrogate markers. Ideally, a direct assessment could be made to determine whether exposure to these drugs is associated with elevated incidence of vascular events. But the hyperlipidemia caused by EIAEDs might easily and incidentally be picked up by primary care physicians performing routine health screening. If the lipid elevation is clinically significant, then treatment with an lipid-lowering agent may be initiated, often with no knowledge that the anticonvulsant is contributing to the problem. This may add to the costs and potential complications of care for patients. It is difficult to assess vascular risk in patients with epilepsy because the excess risk has not been definitively quantified or recognized by the guidelines of learned societies. We suggest the usual risk assessment with consideration that an additional risk may exist in patients with epilepsy. The choice of AEDs may also need to be considered in patients with metabolic or other vascular risk factors.

The Framingham risk score (FRS) is a simplified and common tool for the assessment of risk level of CAD over 10 years. The FRS considers six coronary risk factors, including age, gender, total cholesterol (TC), high density lipoprotein cholesterol (HDL), smoking habits, and systolic blood pressure. FRS is the most applicable method for predicting the person's chance of developing cardiovascular disease (CVD) in long term. Because this risk score gives an indication of the likely benefits ofprevention, it can be useful for both the patients and clinicians deciding whether lifestyle modification and preventive medical treatment and for patients education by identifying men and women at increased risk for future cardiovascular events.

Evidence of a link between epilepsy and increased CVD morbidity and mortality, has been available for several decades. Despite that, there is still a substantial need for definitive recommendations to optimize prevention for these patients.

OBJECTIVES

- To study the prevalence of cardiovascular risk and use of lipid lowering drugs like statins in patients with epilepsy.
- To measure the impact of antiepileptic drugs on quality of life of patients with epilepsy.
- To evaluate the effects of AED polypharmacy on quality of life.

PLAN OF THE STUDY

Phase 1

- To obtain consent from the hospital authorities to carry out the study at the intended department.

Phase 2

- To document all the epilepsy cases which satisfy the inclusion criteria and cases which are admitted in the Department of Neurology of multi-specialty hospital.

Phase 3

- To analyse the statins prescriptions and evaluate the 10 year cardiovascular risk of patients prescribed with statins by using Framingham risk score.
- To evaluate the health related quality of life of patients with epilepsy and understand the effect of AED polypharmacy on QOL.

Phase 4

- To perform the statistical analysis on the collected data to ensure the reliability and acceptability of the data.

METHODOLOGY

The study was carried out in a 1000 bedded multispeciality tertiary care teaching hospital in Coimbatore. The hospital is unique and well known for its service to the people who come from various part of the country. The institution excels in diverse specialities like General medicine, General surgery, Obstetrics, Gynecology, Paediatrics and Neonatology, Orthopedics, Psychiatry, Neurology, Radiology, Cardiology, Nephrology, E.N.T, Opthalmology, Oncology, Dentistry, Plastic surgery, and department of physical rehabilitation. The hospital has well- staffed Pharmacy and a Drug Information Centre. The hospital is well equiped with modern diagnostic facilities like CT scan, MRI, ECG, tread mill, colour doppler,etc. The hospital also have twelve well equiped Hi-tech operation theatres , Intensive Care Unit, Intensive cardiac unit, Intensive pulmonary care unit, NICU, Catheterisation laboratory performing diagnostic cardiac catheterisation, balloon valvuloplasty, coronary stenting, kidney transplantation unit with hemodialysis machines, assisted reproductive technology centre, 24 hour micrbiological and pathological services, blood bank, round the clock casuality and pharmacy services .

DEPARTMENT SELECTED FOR THE STUDY

The study was conducted in the department of neurology. The reason for the selection of the department of neurology was that the pilot study revealed more scope for the study in the department of neurology as the prevalence of epilepsy cases are more. When prescribing, the knowledge on the different types of co-morbidities prevailing and accordingly changes required in treating various stroke study cases in the hospital will help the healthcare professionals to select the appropriate drugs to ensure rational therapy. The study was conducted with expert guidance of the clinical pharmacy professionals and senior neurologist of the study hospital. Prior permission was also obtained from the chief of the concerned department.

CONSENT FROM HOSPITAL AUTHORITIES

A protocol of the study which includes the objectives, methodology an probable outcome was prepared and submitted to the Institutional Ethical Committee. The approval from the committee was procured and the same is attached to reference in the Annexure 1. The study was conducted with the expert guidance of senior and junior physicians of the study departments. The authors were allowed to utilize the hospital facilities to make a follow

up of the cases, in the selected departments. All the health care professionals of the study site were well informed through Dean's official circular.

LITERATURE SURVEY

An extensive literature survey was carried out regaeding the study entitled "*A prospective, observational study on prevalence of cardiovascular risk factors and statin use in patients with epilepsy and assessment of quality of life".* The literatures were collected from various journals including:

- European journal of neurology
- British journal of clinical pharmacology
- Journal of basic and clinical pharmacy
- American journal of family medicine
- Journal of clinical neurology
- International league against epilepsy
- Seizure journal
- Neurology Asia
- Research in neurology
- Journal of neuroscience in rural practice
- Neurology India
- Annals of Indian academy of neurology

PATIENT SELECTION

Inclusion criteria

Patients of either sex admitted in the neurology department during the study period and are receiving drugs for the management of epilepsy with no history of previous cardiovascular events.

Exclusion criteria

Patients who were not diagnosed with epilepsy and those with insufficient data in their records. Pregnant and lactating women were excluded.

STUDY DESIGN

A prospective cross sectional study was carried out in the neurology department to find the prevalence of cardiovascular risk and quality of life in patients with epilepsy. Patients who have been diagnosed with epilepsy were selected as per inclusion criteria. A standardised patient profile form to document the data was designed to collect demographic details of the study population.

DATA ENTRY FORM :

A specially designed data entry format was prepared and used to record the patients details. Data entry format has the provision to record patient details such as name, age,sex, height, weight, IP.Number, date of admission and discharge, reason for admission, patient medical and medical history, vital signs, laboratory investigations, comorbidities, diagnosis, drug chart, drug interaction monitoring chart. The same is given in the Annexure No.4 for reference.

QOLIE -10-P questionnaire

It is a brief questionnaire to screen aspects of health-related quality of life for persons with epilepsy. The QOLIE- 10 is a simple screening questionnaire that can be completed easily and quickly by patients. The 10 items fall into three distinct topics as (a) medication effects, (b) mental health, and (c) role functioning and seizure worry, all of which pertain to aspects of daily living for persons with epilepsy. The QOLIE-I0 provides individual patients with an opportunity to denote epilepsy-related problems and express their concerns to health-care providers. Unlike diagnostic or laboratory individual functions in the real world (e.g., work and social opportunities, transportation, independent living, worry about seizures) . Screening data have several clinical applications for quality of life: (a) alert physician and clinic staff to common patient concerns, (b) inform patients of problems common for this disorder, and (c) facilitate interaction between and decision making by patient and physician . The 10 simple questions in the QOLIE-10 may serve as a screen for problems. A higher quality of life is reflected by a lower score. Higher the QOL score greater is the impairment of QOL.

FRAMINGHAM RISK SCORE

Framingham risk score was used to know the cardiovascular risk of patients in the study population who were prescribed with lipid lowering drugs. Framingham risk score is a gender specific algorithm used to estimate the 10 year cardiovascular risk of an individual. The Framingham risk score was developed based on the data btained based on the Framingham heart study, to estimate the 10-year riskof developing coronary heart disease. FRS is the most applicable method for predicting the person's chance of developing cardiovascular disease (CVD) in long term.

RESULTS AND DISCUSSION

The work entitled "*A prospective, observational study on prevalence of cardiovascular risk factors and statin use in patients with epilepsy and assessment of quality of life"* was conducted in the department of neurology of a 1000 bedded multispecialty hospital .The study protocol was prepared and submitted to the of the hospital and official approval was obtained to carry out the study after ensuring the scope of ethical committee the study in the department of neurology of the study hospital. After receiving the official approval, the study was conducted for a period for a period of eight months from December 2017 to July 2018 . A total of 130 cases with epilepsy were collected.

The analysis of the study conducted for eight months revealed that there were 79(61%) male patients and 51 (39%) female patients who fit into the inclusion criteria. The age categorization of the study population indicated that maximum number of patients are between the age group of 51-65 (36%) followed by age group of 35-50 (32%). Hypertension (28%) and Diabetes(18%) were the major comorbid conditions among epilepsy patients. Patients with smoking (11%) and drinking (7%) habits were also documented during the study. No patients with previous cardiovascular events were included in the study.

The majority of the patients were diagnosed with generalised tonic clonic seizures(37.5%), followed by partial seizures with secondary generalisation(31%). To find out any rationality in therapy, an attempt was made to know about the concurrent drugs prescribed. The results revealed that proton pump inhibitors (89%), antibiotics (51%), lipid lowering agents (52%) and antiemetics (58%) were the major category of drugs prescribed. Antidiabetic drugs (16%) and antihypertensive drugs (26%) dr were major category of drugs prescribed since high prevalence of hypertension and diabetes was observed as comorbidity in the study population. Levetiracetam (84%),was the maximum prescribed antiepileptic drug in the study department, followed by fosphenytoin (32%),lacosamide (24%) and clobazam (20%).The drug interaction between atorvastatin and pantoprazole was the mostly recorded drug interaction,which was observed in 15 patients with moderate severity.

Among the study population 85(65%) patients were receiving polypharmacy and 45(35%) patients were receiving monotherapy. A total of 68(52%) of patients were receiving lipid lowering drugs, in which 51(39%) patients were having lipid profile data,

The health related quality of life of epilepsy patients were assessed with direct interviewing of the patients with QOLIE-10-P questionnaire. The QOLIE-I0-P provided individual patients with an opportunity to denote epilepsy-related problems and express their concerns to health-care providers. The brevity of this screening tool has the potential of saving time without sacrificing the quality of information collected or interfering with the relationship between the patient and the researcher. The QOLIE- 10-P is a simple screening questionnaire that can be completed easily and quickly by patients. The 10 items fall into three distinct topics as (a) medication effects, (b) mental health, and (c) role functioning and seizure worry, all of which pertain to aspects of daily living for persons with epilepsy. The 11^{th} question enables the patient to express his feelings on the burden of epilepsy on his/her normal life.

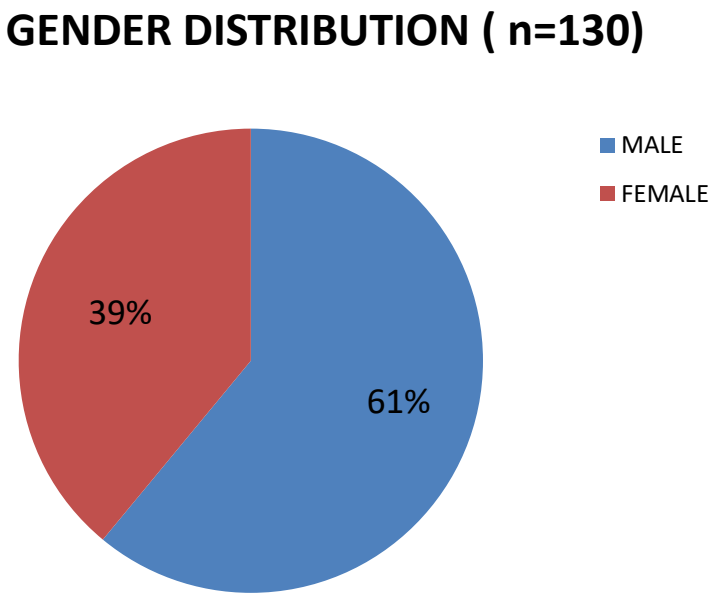
The scoring tool for QOLIE-10-P was obtained from the QOLIE development group and used. The mean score of the first 10 questions were calculated and its mean was multiplied with the score obtained for the 11^{th} question to produce the weighted final score.

The cardiovascular risk and statin use were analyzed for the study population. Framingham risk score was used to analyse the CVD risk of the patients. FRS is the most applicable method for predicting the person's chance of developing cardiovascular disease (CVD) in long term. The FRS considers six coronary risk factors, including age, gender, total cholesterol (TC), high density lipoprotein cholesterol (HDL), smoking habits, and systolic blood pressure. The results obtained were subjected for statistical analysis.

GENDER DISTRIBUTION

The total number of patients in the study were 130 of which 79(61%) were males and 51(39%) were females.The study results showed that mostly males were affected with epilepsy.

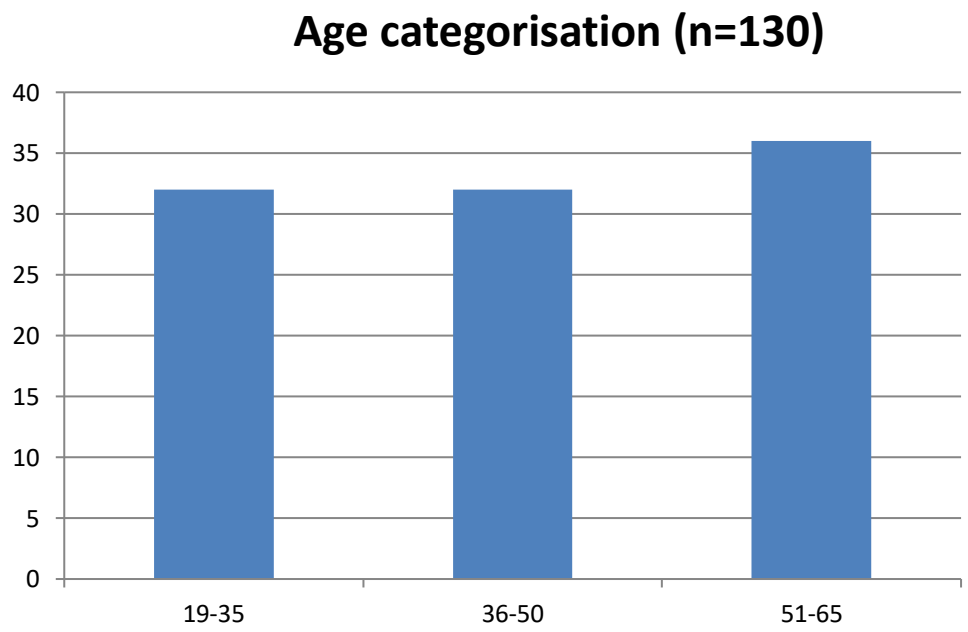
Sex	No. of epilepsy patients	Percentage (%)
Male	79	61
Female	51	39



AGE DISTRIBUTION (n=130)

The study population were categorised based on their age . The obtained results are shown in the below table. The most predominant age group was young adulthood which accounts for about 36% of the overall study population.

Sl.no	Age	Male	Female	No of patients	Percentage
1	Early adulthood (19-35)	23	19	42	32%
2	Adulthood (35-50)	23	19	42	32%
3	Young adulthood (51-65)	33	13	46	36%

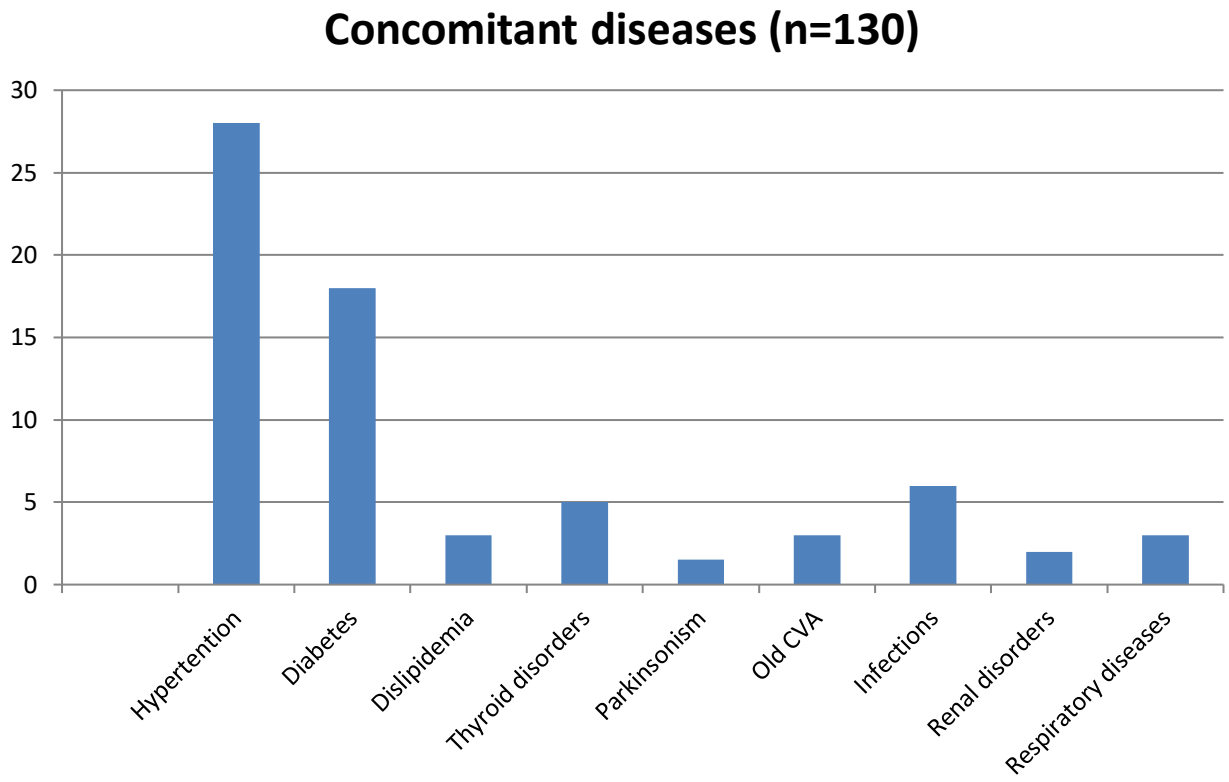


In our study most of the patients were belonging to young adulthood and males were more compared to females . A study conducted by Mintzer et al[23] in 2012 revealed that when patients were categorised into age groups, there was a very significant trend to prescribe AEDs at a higher rate with increasing age . Male patients were significantly more likely to be started on an AED than female patients .

CONCOMITANT DISEASES (n=130)

The co-morbid conditions of the epileptic patients were analyzed and the study population revealed that concomitant diseases like hypertension, diabetes and thyroid disorders were significant.

S.No	Concomitant disease	No. Of patients (%)
1	Hypertension	37(28)
2	Diabetes	24(18)
3	Dislipidemia	4(3)
4	Thyroid disorders	7(5)
5	Parkinsonism	2(1.5)
6	Old CVA	4(3)
7	Infections	8(6)
8	Renal disorders	3(2)
9	Respiratory disorders	4(3)

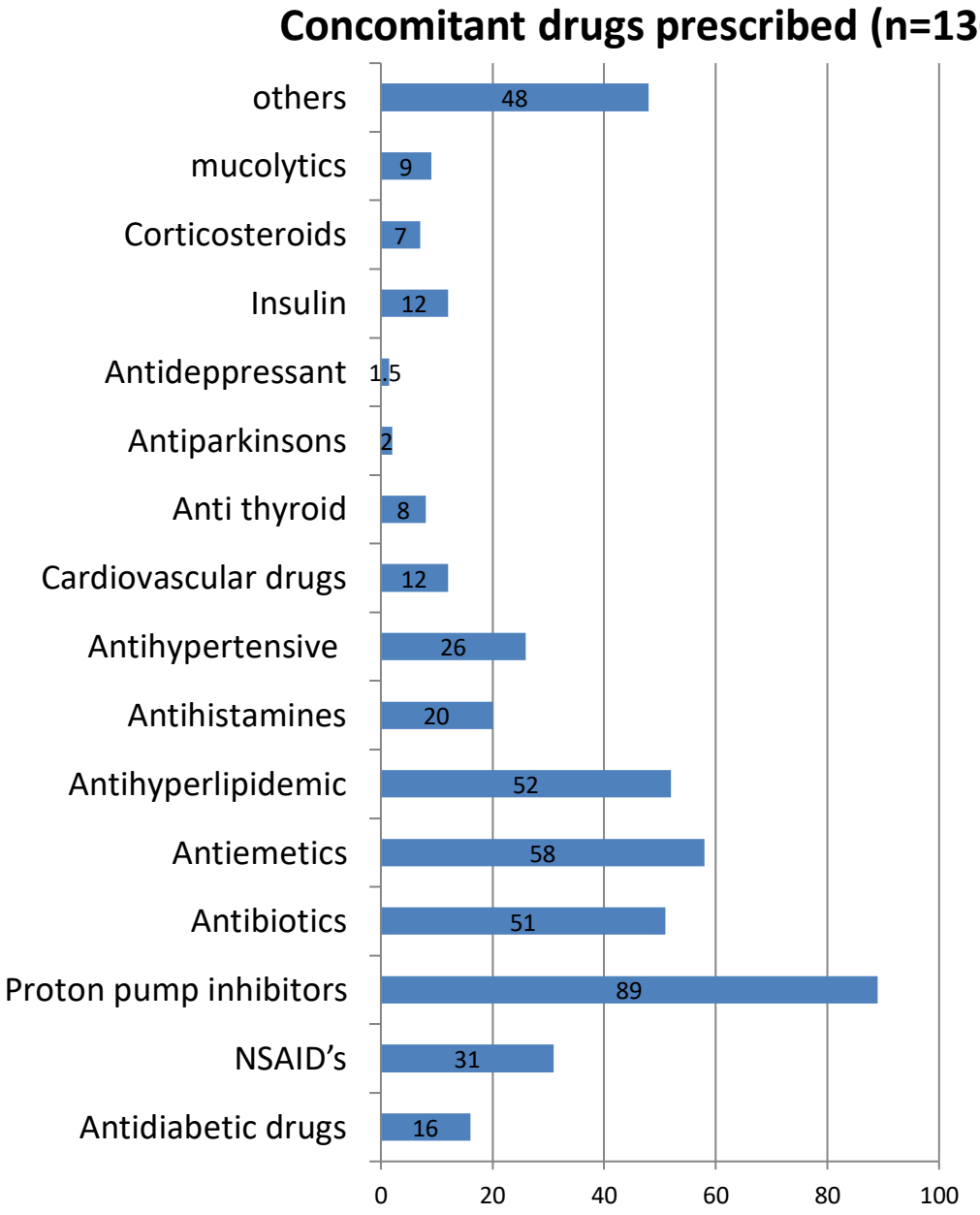


In our study , out of 130 patients 37(38%) were having hypertension and 24(18%) were having diabetes . Similar study conducted by R.M Vivango-Hidalgo et al[4] in 2016 revealed that PWE have been described to have more hypertension and diabetes than the general population, but that finding is inconsistent and both diagnoses are considered risk factors of stroke, a common etiology of epilepsy

CONCURRENT DRUGS PRESCRIBED (n=130)

The concurrent drugs prescribed for epilepsy patients were also analysed in order to understand the rationality of prescription.

DRUGS	No. of patients	Percentage(%)
Antidiabetic drugs	22	16
NSAID's	40	31
Proton pump inhibitors	116	89
Antibiotics	66	51
Antiemetics	76	58
Antihyperlipidemic	68	52
Antihistamines	27	20
Antihypertensive	34	26
Cardiovascular drugs	16	12
Anti thyroid	10	8
Antiparkinsons	3	2
Antideppressant	2	1.5
Insulin	16	12
Corticosteroids	9	7
mucolytics	12	9
others	63	48



Proton pump inhibitors (89%) were the major category on concurrent drugs prescribed, followed by antiemetics (58%) and antihyperlipidemics(52%).

While statins are commonly used for secondary prevention of cardiovascular disease even in the setting of normal cholesterol levels, we excluded any patient with a history of coronary diseases from this portion of the analysis, so it is unlikely that many statin prescriptions in this study population were for this purpose.

A study conducted by mintzer et al 2015[23] revealed that once patients receive new AED therapy forseizures, those prescribed EIAEDs are almost 50% more likely to be subsequently started on lipid-lowering therapy than those who receive non-inducing AEDs.

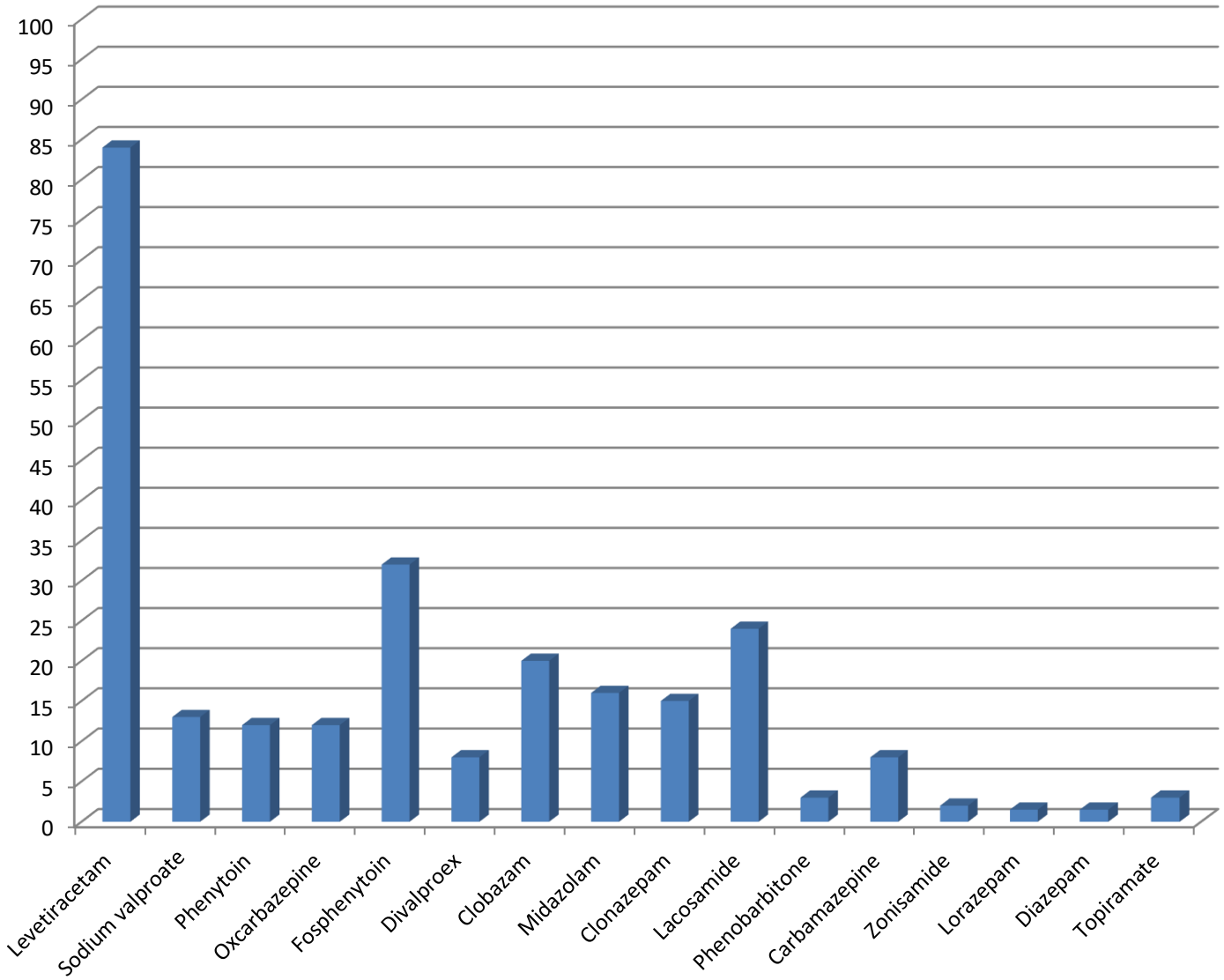
TYPES OF SEIZURES (n=130)

Disease Characteristics Description n (%) n=130	Number of patients	Percentage(%)
Type of Seizures Partial Seizures	76	58
Simple Partial Seizure	19	14
Complex Partial Seizures	17	13
Partial Seizures with secondary generalization	40	31
Generalized Seizures	54	42
Generalized tonic clonic	49	37.5
Absence Seizures	1	0.76
Myoclonic Seizures	4	3.5

The majority of the patients were diagnosed with generalied tonic clonic seizures followed by patients diagnosed with partial seizures with secondary generalisation.

DRUGS PRESCRIBED FOR EPILEPSY (n=130)

DRUGS	No. of patients	Percentage(%)
Levetiracetam	110	84
Sodium valproate	17	13
Phenytoin	14	12
Oxcarbazepine	14	12
Fosphenytoin	42	32
Divalproex	11	8
Clobazam	27	20
Midazolam	21	16
Clonazepam	20	15
Lacosamide	32	24
Phenobarbitone	4	3
Carbamazepine	11	8
Zonisamide	3	2
Lorazepam	2	1.5
Diazepam	2	1.5
Topiramate	5	3



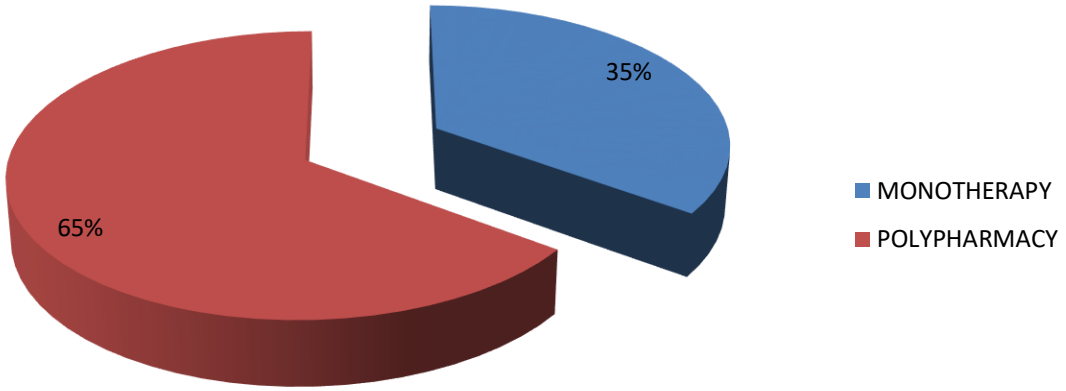
There are many drugs prescribed for epilepsy ,of which levetiracetam was the most prescribed drug having prescribed to over 85% of the patients followed by fosphenytoin (32%) and lacosamide (24%).

DRUG INTERACTION IN THE PRESCRIPTION(n=130)

Sl.no	Interaction drugs	Inferences	severity	No.of patients
1	Atorvastatin+ pantoprazole	Increase the blood levels and effects of atorvastatin	Moderate	15
2	Clopidogrel + pantoprazole	Decrease effects of clopidogrel	Moderate	14
3	Aspirin + telmisartan	Decrease effects of telmisartan in decreasing BP	Moderate	3
4	Aspirin + clopidogrel	May cause unusual bleeding	Moderate	4
5	Aspirin + insulin	Hypoglycemia may be potentiated	Moderate	1
6	Ketorolac + amitriptylline	Concurrent use may lead to incresed risk of bleeding	Major	1
7	Phenytoin + clopidogrel	Increase effect of hepatic CYP3A4 metabolism	Moderate	4
8	Phenytoin + atorvastatin	Decrease effect of hepatic CYP3A4 metabolism	Moderate	6
9	Fosphenytoin + midazolam	Concurrent use result in decreased efficacy of midazolam	Moderate	7
10	Divalproex + fosphenytoin	Concurrent use may result in altered valproate or phenytoin level	Moderate	3
11	Clobazam + paracetamol	Additive respiratory depression	Moderate	1
12	Levetiracetam + paracetamol	Decreases level of paracetamol	Minor	1

POLYPHARMACY AND MONOTHERAPY CATOGORISATION (n=130)

SL NO	CATOGORY	NO OF PATIENTS	PERCENTAGE
1	POLYPHARMACY	85	65%
2	MONOTHERAPY	45	35%



ASSESSMENT OF STATIN USE (n=130)

1	**Patients prescribed with statins**	**68**	**52%**
2	Patients with lipid profile available and prescribed with statins.	51	39%
3	Patients with no lipid profile available and prescribed with statins.	17	13%

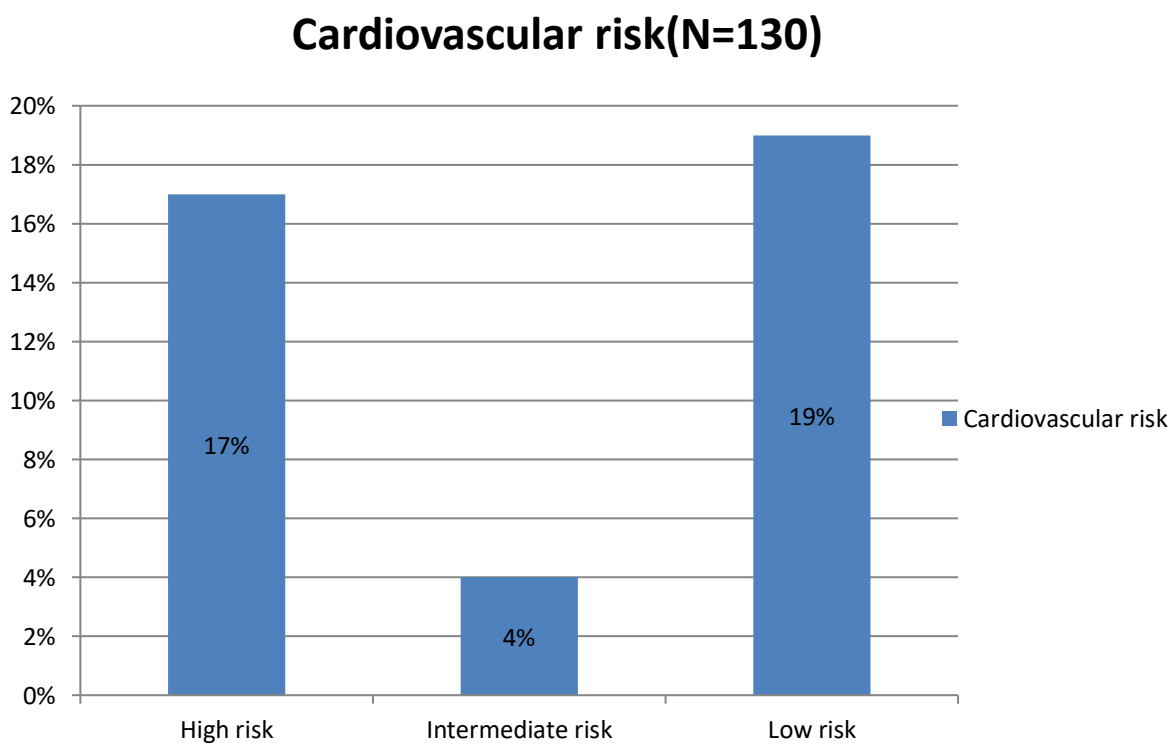
Out of the 130 patients 68 patients were prescribed with statins and 51 patients had done lipid profile. Since 52% of the study population was prescribed with statins . A study conducted by Ane Gedde-Dahl et al[29] in 2012 revealed that the study showed high prevalence of co-prescription of statins with AEDs in Norwegian clinical practice.

CARDIOVASCULAR RISK ASSESSMENT USING FRAMINGHAM RISK(n=130)

Sl no	Cardiovascular risk	No of patients	Percentage %
1	High risk	22	17%
2	Intermediate risk	5	4%
3	Low risk	24	19%

The Framingham risk score was used to analyze the 10 – year cardiovascular risk of the patients. Risk factors included were age, sex, total cholesterol (mg/dl), high-density lipoprotein cholesterol (HDLc, mg/dl), DBP and SBP (mmHg), diabetes and smoking.Risk was categorized as low (<5%), intermediate (5%_9.9%) and high (≥10%).In our study patients with epilepsy showed prevalence of hypertension and diabetes. It was found that this group had more prevalence of diabetes. Smoking was categorised in three groups: current , former and never smokers. Dislipidimia was also prevalent in a few patients.

Patients who was on high risk had high prevalence of hypertension ,diabetes and smoking .



There are some limitations. Since lipid profile was a important factor to assess the cardiovascular risk ,the unavailability of lipid pfofile was a limitation faced during the study. No information was available about lipid levels or cardiovascular risk before AED or statin treatment.

A study conducted by Etminan M et al[29] revealed that the use of statins not only has proven efficacy for CVDs, but also provides an antiepileptogenic effect and may decrease the risk of epilepsy hospitalization in cardiovascular patients .

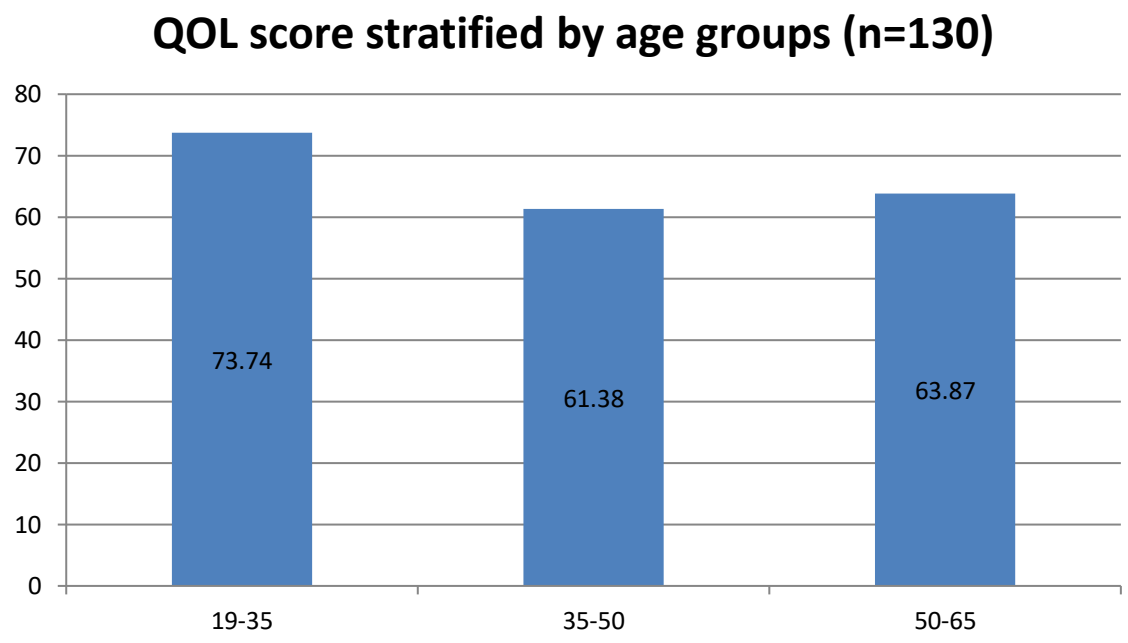
QUALITY OF LIFE ASSESSMENT

The QOLIE-10 questionnaire was used to measure the overall quality of life in study sample. The QOLIE-10-P screening questionnaire scoring instructions was obtained from the author. The QOLIE-10-P is a patient weighted questionnaire ,which provides a weighted final score . Higher scores represent better quality of life.

QUALITY OF LIFE STRATIFIED BY AGE GROUP(n=130)

The final QOL score was stratified by age group and the patients belonging to early adulthood was having a relatively high QOL.

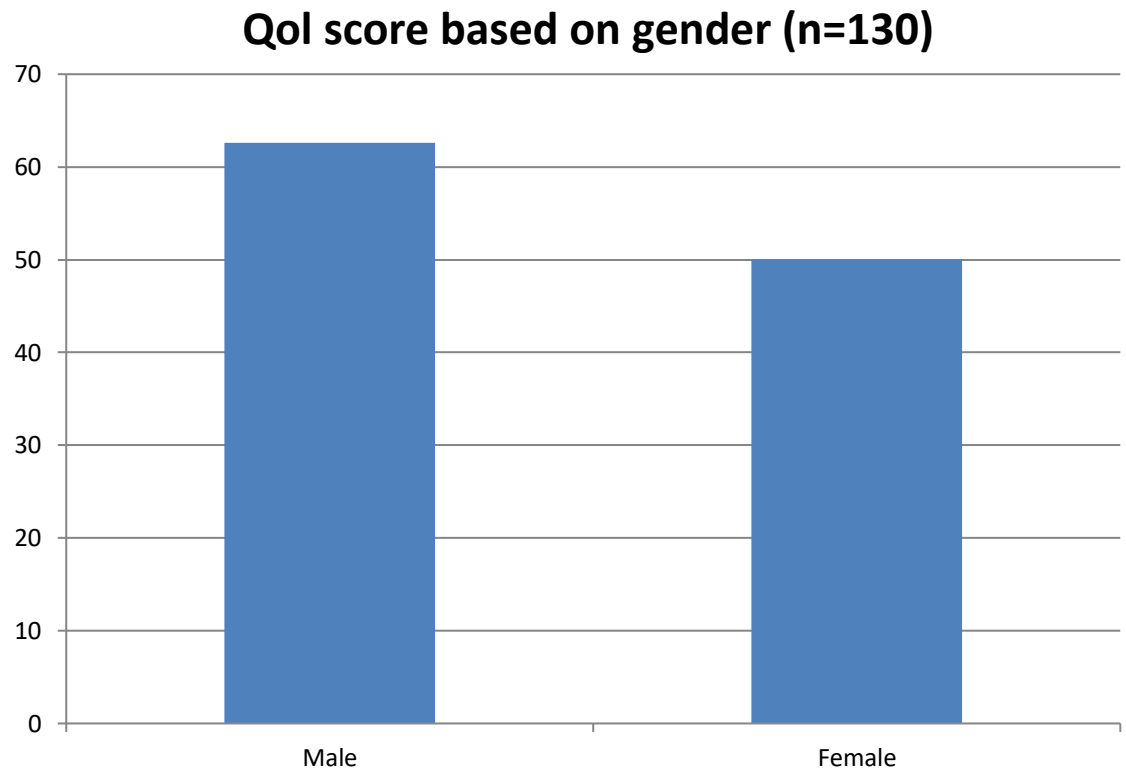
Sl no	Age groups	Mean QOL score	SD
1	Early adulthood (19-35)	73.74	12.6289
2	Adulthood (35-50)	61.38	5.1336
3	Late adulthood (50-65)	33.87	1.2304



The QOL score obtained for different age groups were statistically analysed by using one-way ANOVA. The f-ratio value is 13.77851. The p-value is .030762. The result is significant at p<.05.this means that the difference between QOL scores obtained by different age groups are statistically significant.

QUALITY OF LIFE SCORES STRATIFIED BY GENDER

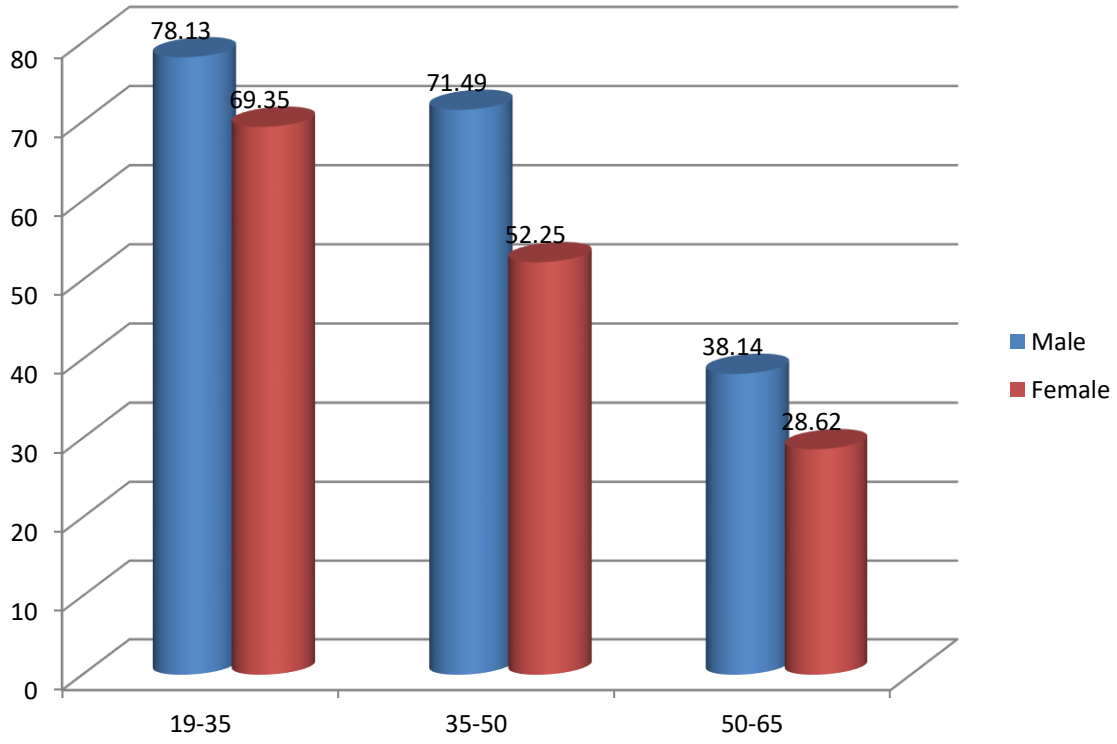
Sl no	Gender	QOL score
1	Male	62.58
2	Female	50.07



The younger males had a good QOL score and elder females had the worst quality of life score.

COMPARISON OF QOL SCORE BETWEEN GENDER AND DIFFERENT AGE GROUP (n=130)

Sl no	Age group / Gender	Earlyadulthood (19-35)	Adulthood (35-50)	Late adulthood (50-65)
1	Male	78.13	71.49	38.14
2	Female	69.35	52.25	28.62



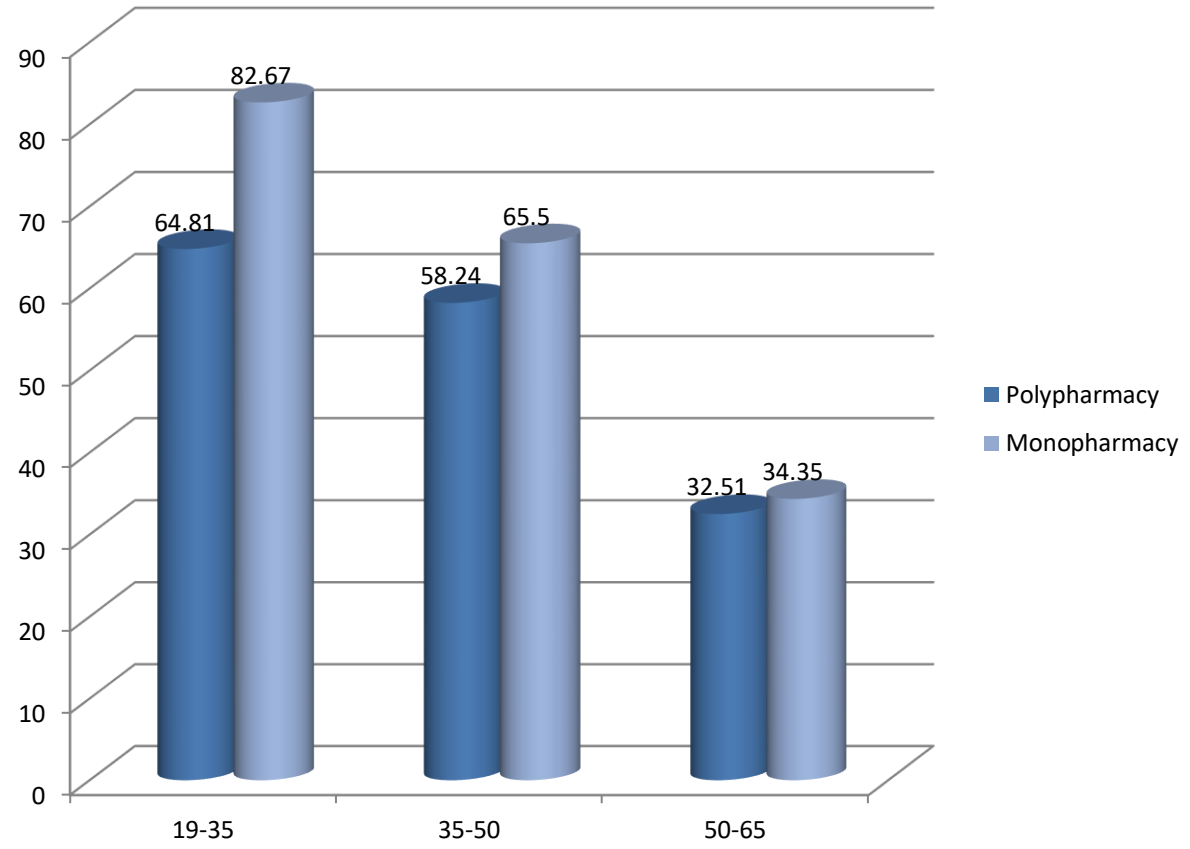
Out of 130 patients 79(61%) were males and 51(39%) were females. In our study male patients had better quality of life score than females. Increasing age also showed greater impairment of QOL. Prakruti Patel et al in 2017[(5)] revealed that that males had higher QOL score compared to females as it was found that male enrolled in study had higher education than females, thus contributing to better QOL. We also noted that QOL score was found to decrease with increasing age most probably due to chronicity of disease and drug therapy thus effecting QOL.

COMPARISON OF MEAN SCORE OF QOL BETWEEN POLYPHARMACY AND MONOTHERAPY (n=130)

Sl no	Age groups	Polypharmacy	Monopharmacy
1	Early adulthood 19-35	64.81	82.67
2	Adulthood 35-50	58.24	65.50
3	Late adulthood 50-65	32.51	34.35

According to a recent study conducted by Halley B Alexander et al in 2017[11] revealed that patients on polypharmacy were almost twice likely to have continuing seizures than monotherapy patients. They also had worse QOL scores , most prominently on epilepsy effect and role functioning domains.

The QOL score obtained by patients receiving polypharmacy and monopharmacy were statistically analysed using unpaired student t-test. The p-value obtained was 0.634,ie p-value is greater than .05. This means that the difference is not statistically significant



Out of 130 patients 85 were on polytherapy and 45 were on monotherapy. The adverse drug reactions caused by AEDs can be the cause of poor QOL of patients on polytherapy. A study conducted by R K Surekha et al in the year 2015[(12)] revealed that patients who were on a single drug (monotherapy) had a much better QOL than the patients on more than one drug (polytherapy). The type of drug therapy followed by a patient with epilepsy plays a very important role. Patients who were on monotherapy had a better quality of life mainly because of the lesser side effects as compared with those on polytherapy.

SUMMARY

The work entitled " A prospective, observational study on prevalence of cardiovascular risk factors and statin use in patients with epilepsy and assessment of quality of life*"* was conducted in the department of neurology of a 1000 bedded multispecialty hospital .The study protocol was prepared and submitted to the ethical committee of the hospital and official approval was obtained to carry out the study after ensuring the scope of the study in the department of neurology of the study hospital. After receiving the official approval, the study was conducted for a period for a period of eight months from December 2017 to July 2018. The results obtained from the study population are summarized as follows:

- The study population consisted of 130 patients with epilepsy as per the inclusion criteria.
- There were 79(61%) male patients and 51 (39%) female patients included in the study.
- The maximum number of patients were between the age group of 51-65 (36%) followed by age group of 35-50 (32%).
- Hypertension (28%) and Diabetes(18%) were the major comorbid conditions among epilepsy patients.
- The majority of the patients were diagnosed with generalised tonic clonic seizures(37.5%), followed by partial seizures with secondary generalisation(31%).
- Proton pump inhibitors (89%), antibiotics (51%), lipid lowering agents (52%) and antiemetics (58%) were the major category of drugs prescribed.
- Antidiabetic drugs (16%) and antihypertensive drugs (26%) dr were major category of drugs prescribed since high prevalence of hypertension and diabetes was observed as comorbidity in the study population.
- Levetiracetam (84%),was the maximum prescribed antiepileptic drug in the study department, followed by fosphenytoin (32%),lacosamide (24%) and clobazam (20%).
- The drug interaction between atorvastatin and pantoprazole was the mostly recorded drug interaction,which was observed in 15 patients with moderate severity.

- In the study population 85(65%) patients were receiving polypharmacy and 45(35%) patients were receiving monotherapy.
- In the study population 68(52%) of patients were receiving lipid lowering drugs, in which 51(39%) patients were having lipid profile data.
- In the study population 22(17%) patients were with high cardiovascular risk and 24 (19%) patients were with low cardiovascular risk.
- The patients belonging to early adulthood was having a relatively high QOL.
- The younger males had a good QOL score and elder females had the worst quality of life score.
- Out of 130 patients 79(61%) were males and 51(39%) were females. In our study male patients had better quality of life score than females. Increasing age also showed greater impairment of QOL.
- Patients who were on monotherapy had a better quality of life mainly because of the lesser side effects as compared with those on polytherapy.

CONCLUSION

The health related quality of life includes health factors that both positively and negatively impact the quality of life. There is a lack of knowledge regarding the health related quality of life among individuals living with epilepsy at the community level and the factors associated with poor quality of life in a rural population. The protective as well as risk factors for the poor quality of life if known can help direct future research to formulate more effective strategies to help individuals and their patients to cope with the disease thus improving their quality of life and decrease the burden on individuals, their families and the community.

The majority of the patients included in the study were males (61%) and females(39%). Most of the patients were males and patients belonged to the age group of 50-65 years. Younger males had better QOL scores and elder females had the worst QOL scores. The increase in the age showed increase in the impairment of quality of life. Patients receiving monopharmacy had better QOl scores when compared to polypharmacy group. This may be due to the impact of side effects of antiepileptic drugs used.

The use of lipid lowering drugs like statins was found to be higher in patients with epilepsy regardless of the serum lipid levels. Among patients prescribed with statins most of the patients were at low risk of cardiovascular disease. Recent studies suggest that enzyme inducing AEDs may alter the serum cholesterol levels. So switching over to non-enzyme inducing AEDs may help in stabilising the serum lipid levels and CVD risk of patients with epilepsy.

FUTURE OUTLOOK

The present study covers the health related quality of life and assess the prevalence of cardiovascular risk factors and statin use in patients with epilepsy. QOLIE-10-P questionnaire which is an abbreviated quality of life questionnaire for epilepsy was administered to each patient to measure their overall QOLIE-10 score.

The possible interventions can be divided into interventions to improve the control over epilepsy, to decrease the side effects of the medications, to improve the coping skills of individuals with epilepsy and better management of comorbidities. Interventions to improve control over epilepsy can include changing medications to newer anti-epileptic medications, which have fewer side effects but cost is a major limitation. The State run Public Health System can play an important role in addressing this issue.

Future aspects of the study may be include interviewing patients in multiple stages ie, atthe time of admission, during recovery periods as 3rd month, 6th month etc. Such studies can evaluate the improvements achieved due to the interventions made by the pharmacist. There is also a great need for further research in to interventions for occupational therapy, as socioeconomic status and occupation were factors that had influence on the quality of life.

Appropriate AED selection preferably monotherapy and careful evaluation of drug side effects play a crucial role in achieving the ultimate target goals of seizure freedom and optimal quality of life among patients with epilepsy.

Ideally, a cardiovascular risk score should be calculated in those receiving no treatment at the start of and during the study. Physicians should use clinical judgement to decide on further treatment of CVRFs in PWE who are below the recommended risk threshold for treatment and should consider lipid abnormalities a potential side-effect of EIAEDs. Other therapy options may need to be evaluated before starting lipid-lowering treatment.

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Case No.

DEPARTMENT OF PHARMACY PRACTICE
College of Pharmacy, SRIPMS, Coimbatore - 44.

A PROSPECTIVE, STUDY ON PREVALENCE OF CARDIOVASCULAR RISK FACTORS AND STATIN USE IN PATIENTS WITH EPILEPSY AND ASSESSMENT OF QUALITY OF LIFE

DATA ENTRY FORM

PATIENT DETAILS									
Name	Age	Sex	Wt.	Ht.	BMI	IP No.	Dept.	DOA	DOD

REASONS FOR ADMISSION

PAST MEDICAL HISTORY

PAST MEDICATION HISTORY

Vital Signs											**Blood sugar (mg %)**									
Date											**Day**									
Temp.											F.B.S (70-100)									
BP											P.P.S (<140)									
Pulse											R.B.S (70-140)									

BLOOD COUNTS						
Haemoglobin (g/dl) M:14-18 F:12-14	TLC (cells/cumm) (6000-10000)	ESR (mm/hr) (M<10; F<20)	Differential Leukocyte Count (%)			
			Polymorphs (40-75)			
			Lymphocytes(20-45)			
Platelets (1-4 lakhs)	Clotting Time(6-11min)	Bleeding Time(1-6min)	Basophils (0-1)			
			Eosinophils (1-6)			
			Monocytes (2-10)			

LIVER FUNCTION TESTS								**RENAL FUNCTION TESTS**			
Total bilirubin (0.1-1.2 mg %)				Alk. Phosphatase (38-126 U/L)				Urea (mg %) (12-35)			
								Uric acid (mg %) F-2.4-5.7, M-3.4-7			
P.T Time (12-15 sec)				SGPT (9-52U/L)				Sr.Creatinine (mg %) (0.4-1.4)			

ELECTROLYTES (mEq/l)					**URINE EXAMINATION**			
Sodium (130-150)					Colour		Sugar	
Potassium (3.5 – 5.8)					Bile salts		WBC	
Chloride (95-105)					Bile pigment		RBC	
Bicarbonate (22-39)					Albumin		Casts	
					Pus cells		Epithelial cells	

COMORBIDITIES			
Hypertension ☐	**Dyslipidemia ☐**	**Cardiovascular risk factors ☐**	
Blood disorder ☐	**diabetes Mellitus ☐**	**Asthma ☐**	**Others ☐**

LIPID PROFILE				
Total cholestrol				
HDL cholestrol				
LDL cholestrol				
Triglycerides				

OTHER INVESTIGATIONS:

DIAGNOSIS:

DRUGS PRESCRIBED

S.No.	Drugs		Strength	Route of admin.	Days of Treatment											
	T. Name	G. Name														
01																
02																
03																
04																
05																
06																
07																
08																
09																
10																
11																
12																
13																
14																
15																

DRUG INTERACTIONS

DRUGS	EFFECT	SEVERITY	INFERENCE

ANY INTERVENTIONS MADE

NAME OF THE INVESTIGATOR:BINIL BABY

SUBMISSION DATE:

Signature of the investigator **Signature of the staff**

FRAMINGHAM RISK SCORE (FRS)

Estimation of 10-year Cardiovascular Disease (CVD) Risk

Date: _____

Patient's Name: _____

Step 1[1]

In the "points" column enter the appropriate value according to the patient's age, HDL-C, total cholesterol, systolic blood pressure, and if they smoke or have diabetes. Calculate the total points.

Risk Factor		Risk Points				Points
		Men		Women		
Age						
30-34		0		0		
35-39		2		2		
40-44		5		4		
45-49		7		5		
50-54		8		7		
55-59		10		8		
60-64		11		9		
65-69		13		10		
70-74		14		11		
75+		15		12		
HDL-C (mmol/L)						
>1.6		-2		-2		
1.3-1.6		-1		-1		
1.2-1.3		0		0		
0.9-1.2		1		1		
<0.9		2		2		
Total Cholesterol						
<4.1		0		0		
4.1-5.2		1		1		
5.2-6.2		2		3		
6.2-7.2		3		4		
>7.2		4		5		
Systolic Blood Pressure (mmHg)		Not Treated	Treated	Not Treated	Treated	
<120		-2	0	-3	-1	
120-129		0	2	0	2	
130-139		1	3	1	3	
140-149		2	4	2	5	
150-159		2	4	4	6	
160+		3	5	5	7	
Diabetes	Yes	3		4		
	No	0		0		
Smoker	Yes	4		3		
	No	0		0		
Total Points						

[1] Adapted from: D'Agostino RB et al.(i). General cardiovascular risk profile for use in primary care. The Framingham Heart Study. Circ 2008;117:743-53.
[2] Adapted from: Genest J et al.(i). 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult. Can J Cardiol. 2009;25(10):567-579.
[3] Adapted from: Anderson T et al.(i). 2012 Update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol. 2013;29(2):151-167.

Step 2[1]

Using the total points from Step 1, determine the 10-year CVD risk (%).*

Total Points	10-Year CVD Risk (%)*	
	Men	Women
-3 or less	<1	<1
-2	1.1	<1
-1	1.4	1.0
0	1.6	1.2
1	1.9	1.5
2	2.3	1.7
3	2.8	2.0
4	3.3	2.4
5	3.9	2.8
6	4.7	3.3
7	5.6	3.9
8	6.7	4.5
9	7.9	5.3
10	9.4	6.3
11	11.2	7.3
12	13.3	8.6
13	15.6	10.0
14	18.4	11.7
15	21.6	13.7
16	25.3	15.9
17	29.4	18.51
18	>30	21.5
19	>30	24.8
20	>30	27.5
21+	>30	>30

* Double cardiovascular disease risk percentage for individuals between the ages of 30 and 59 without diabetes if the presence of a positive history of premature cardiovascular disease is present in a first-degree relative before 55 years of age for men and before 65 years of age for women. This is known as the modified Framingham Risk Score.[3]

Step 3[1]

Using the total points from Step 1, determine heart age (in years).

Heart Age, *y*	Men	Women
<30	<0	<1
30	0	
31		1
32	1	
34	2	2
36	3	3
38	4	
39		4
40	5	
42	6	5
45	7	6
48	8	7
51	9	8
54	10	
55		9
57	11	
59		10
60	12	
64	13	11
68	14	12
72	15	
73		13
76	16	
79		14
>80	≥17	15+

Step 4[2,3]

Using 10-year CVD risk from Step 2, determine if patient is Low, Moderate or High risk.† Indicate Lipid and/or Apo B targets

Risk Level†	Initiate Treatment If:	Primary Target (LDL-C)	Alternate Target
High FRS ≥20%	• Consider treatment in all *(Strong, High)*	• ≤2 mmol/L or ≥50% decrease in LDL-C *(Strong, Moderate)*	• Apo B ≤0.8 g/L or • Non-HDL-C ≤2.6 mmol/L *(Strong, High)*

Intermediate
FRS 10-19%
	• LDL-C ≥3.5 mmol/L *(Strong, Moderate)*
	• For LDL-C <3.5 mmol/L consider if:
	  • Apo B ≥1.2 g/L
	  • OR Non-HDL-C ≥4.3 mmol/L *(Strong, Moderate)*
		• ≤2 mmol/L or ≥50% decrease in LDL-C *(Strong, Moderate)*	• Apo B ≤0.8 g/L or
			• Non-HDL-C ≤2.6 mmol/L *(Strong, Moderate)*

Low FRS <10%	• LDL-C ≥5.0 mmol/L • Familial hypercholesterolemia *(Strong, Moderate)*	• ≥50% decrease in LDL-C *(Strong, Moderate)*	N/A

Lipid targets LDL-C: _____ or Apo B: _____

† Consider moving some patients with metabolic syndrome up a risk level based on their 'load' of metabolic risk factors or the 'severity' of their metabolic syndrome.
‡ Atherosclerosis in any vascular bed, including carotid arteries.
apoB: apolipoprotein B stat; CAD: coronary artery disease; FRS: Framingham Risk Score; HDL-C: high-density lipoprotein cholesterol; hs-CRP: high-sensitivity C-reactive protein; PVD: peripheral vascular disease; RRS: Reynolds Risk Score; TC: total cholesterol.

Provided courtesy of
Canadian Cardiovascular Society
Leadership. Knowledge. Community.

COLLEGE OF PHARMACY
Sri Ramakrishna Institute of Paramedical Sciences
Sri Ramakrishna hospital campus 395, sarojini naidu road
Coimbatore-641044

PATIENT CONSENTFORM

I_____ have been made understood the necessity of the work entitled **"A prospective, observational study on prevalence of cardiovascular risk factors and statin use in patients with epilepsy and assessment of quality of life"** that is being carried out by **Binil Baby,** II year M.Pharm, (Pharmacy Practice) in College of Pharmacy, SRIPMS, Coimbatore. I voluntarily hereby agree by giving my consent to participate in this study and provide the necessary co-operation for the same.

Place: Coimbatore
Date:

Signature of the Patient/By-stander

Name of the Patient:
Name of the By-stander:

Signature of the Supervisor

Dr S .Sriram ,M.Pharm, Ph D.,
Professor & HOD,
Department of Pharmacy Practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

Signature of the Investigator

Binil Baby
II M. Pharm., Pharmacy Practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

THE QOLIE DEVELOPMENT GROUP
Permission for use of the QOLIE-10-P

Joyce Cramer, for the QOLIE Development Group

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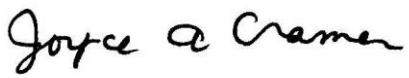


Joyce A Cramer
For the QOLIE Development Group

Patient Weighted Quality Of Life In Epilepsy:
QOLIE-10-P

Today's Date _____/_____ / _____ mm dd yy	Your Name_____ Your Age: ___ ___ years

INSTRUCTIONS

The QOLIE-10-P is a brief survey of health-related quality of life for adults with epilepsy. There are 10 questions about health and daily activities, one question about how much distress you feel about problems and worries related to epilepsy, and a review of what bothers you most. This questionnaire should be completed only by the person who has epilepsy (not a relative or friend) because no one else knows how YOU feel.

Answer every question by circling the appropriate number (1, 2, 3...). If you are unsure about how to answer a question, please give the best answer you can and write a comment or explanation on the side of the page. These notes may be useful if you discuss the QOLIE-10-P with your doctor. Completing the QOLIE-10-P before and after treatment changes may help you and your doctor understand how the changes have affected your life.

These questions are about how you have been FEELING and the types of problems you have been having during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks… *(Circle one number on each line)*

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
1. Did you have a lot of **energy**?	**1**	**2**	**3**	**4**	**5**	**6**
2. Have you felt **downhearted and low**?	**1**	**2**	**3**	**4**	**5**	**6**

3. How much of the time during the past 4 weeks your epilepsy or antiepileptic drugs have caused trouble with **driving (or other transportation)**

A great deal	A lot	Somewhat	Only a little	Not at all
1	**2**	**3**	**4**	**5**

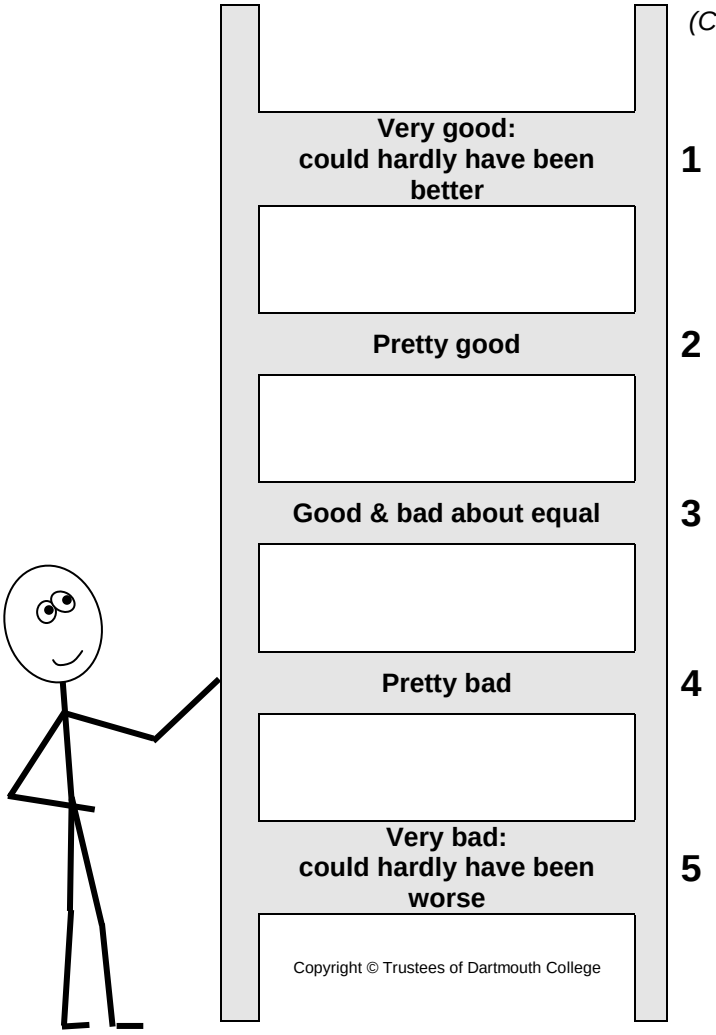
During the past 4 weeks…	Not at all bothersome				Extremely bothersome
4. How much do your **work limitations** bother you?	**1**	**2**	**3**	**4**	**5**
5. How much do your **social limitations** bother you?	**1**	**2**	**3**	**4**	**5**

During the past 4 weeks…	Not at all bothersome				Extremely bothersome
6. How much do your **memory difficulties** bother you?	**1**	**2**	**3**	**4**	**5**
7. How much do **physical effects** of antiepileptic drugs bother you?	**1**	**2**	**3**	**4**	**5**
8. How much do **psychological effects** of antiepileptic drugs bother you?	**1**	**2**	**3**	**4**	**5**

	Very afraid	Somewhat afraid	Not very afraid	Not afraid at all
9. How **afraid** are you of having a seizure during the next 4 weeks?	**1**	**2**	**3**	**4**

10. How has your **QUALITY OF LIFE** been during the **past 4 weeks** (that is, how have things been going for you)?

(Circle one number on the ladder)



Reviewing all the questions you have answered above, consider the overall impact of these problems on your quality of life ***in the past 4 weeks*****.** *(Circle one number)*

	Not at all	Somewhat	Moderately	A lot	Very much
11. How much does the state of your epilepsy-related quality of life **distress** you overall?	**1**	**2**	**3**	**4**	**5**

Considering ***ALL*** *the questions you have answered, please* ***indicate the areas*** *related to your epilepsy that are most* ***IMPORTANT*** *to you* ***NOW.***

12. *Number the following topics from '1' to '7' with '1' corresponding to the most important topic and '7' to the least important one. Please use each number only once.*

⌊___⌋ **A.** Energy (tiredness)

⌊___⌋ **B.** Emotions (mood)

⌊___⌋ **C.** Daily activities (work, driving, social & other activities)

⌊___⌋ **D.** Mental function (thinking, concentrating, memory)

⌊___⌋ **E.** Medication effects (physical, mental)

⌊___⌋ **F.** Worry about seizures (impact of seizures)

⌊___⌋ **G.** Overall quality of life

This copy of the QOLIE-10-P is provided by the QOLIE Development Group.We wish you success in living your life with epilepsy!

Quality of Life In Epilepsy: QOLIE-10-P
SCORING INSTRUCTIONS

Provided by the QOLIE Development Group
Contact person: joyce.cramer@gmail.com

The QOLIE-10 screening questionnaire includes 11 questions. Three questions have opposite response sets, requiring reverse-scoring. The scoring should be calculated so that all positive responses are lower numbers and all negative responses are higher numbers.
[The QOLIE-10-P includes 11 questions, with items 1-10 identical to the QOLIE-10.]

Patients with lowest scores have the least problems. Thus, some items must be reverse-scored to reflect higher quality of life:
Items scored with "1" as best should be scored in "reverse":
Items scored with "1" as worst should be scored as indicated:

		1	2	3	4	5	6	Item Score	
	1	100	80	60	40	20	0		
	2	0	20	40	60	80	100		
	3	0	25	50	75	100			
	4	100	75	50	25	0			
	5	100	75	50	25	0			
	6	100	75	50	25	0			
	7	100	75	50	25	0			
	8	100	75	50	25	0			
	9	0	33.3	66.7	100				
	10	100	75	50	25	0			
							Subtotal =		
							Mean Score=Subtotal ÷ 10 =		
Distress									
	11	100%	75%	50%	25%	10%	**Distress Score (%)**		**%**
							Final Score (Mean x Distress%)		

CALCULATIONS:

1. The Mean Score is the sum of scores for all questions divided by the number of items answered.
2. The Mean Score is multiplied by the response for Item # 11 to create the final “weighted” score.
3. If one item is missing, the score may be imputed based on the 9 responses. If more than one item is missing, the instrument is not valid.
4. Higher scores represent better quality of life.

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